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TOTAL BODY POTASSIUM AND GROSS BODY COMPOSITION IN RELATION TO AGE*

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Rubner (26) long ago introduced the concept of an "active tissue mass," and postulated a relationship between this mass and body heat production. Because of its intracellular occurrence, potassium may offer a rather direct measure of this quantity. Potassium is usually the most abundant of the cations found inside living cells of vertebrates (20); a small quantity also occurs in extracellular fluids. Potassium participates in propagation of nerve impulses, is involved with muscular contraction, and is recognized as necessary for biocatalysis. It is excreted chiefly by the kidneys and is replenished by ingestion of food. A detailed theory explaining accumulation of potassium by living matter (especially in muscle cells) has been proposed by Conway (12).

Although the importance of potassium in a number of vital processes is well established, it has been difficult to determine the total quantity in the body. Direct analyses are available for only a limited number of cases. Results of chemical analysis of two cadavers by Forbes and Lewis (17) indicate that about 60% of all body potassium is contained in muscle.

The determination of body potassium by isotopic dilution using K^{42} as a tracer (13) is nondestructive and can be applied *in vivo* but is time consuming, and the requirement of ingestion of radio-activity limits its applicability. This method determines exchangeable, not total, potassium, but the evidence is that if sufficient mixing time is allowed (48 hours) the two quantities are very similar.

The first direct measurements of total body potassium by means of its natural radioactivity were made by Sievert (28, 29) and by Burch and Spiers (11). Sievert (29) and Sagild (27) established the change in body potassium content with age and indicated its explanation. These early studies used ionization chambers to measure the 1.46-Mev gamma rays from the K^{40}, which occur in constant proportion in all normal potassium. Development of the low background sodium iodide crystal spectrometer (21, 24) reduced the time required for such measurements and improved the precision of body potassium determinations.

Measurements can be made even more rapidly with a 4π liquid scintillation counter (4, 5, 31), which can quantify total body potassium to a precision of 2% in less than 200 seconds of counting time. Using the liquid scintillation counter, Anderson and Langham (7) reported body potassium measurements in 1590 subjects of both sexes, ranging in age from less than 1 year to 79 years. The average concentration of potassium per kilogram of gross body weight showed interesting correlations with age and sex, one of the prominent features being a steady decline with increasing age for adults. Confirmation of the general features of the curve and excellent quantitative agreement for two additional large population groups (one American, one German) have been obtained with other liquid scintillation counters (25, 33).

Where large enough population groups have been measured to permit accurate comparisons, agreement among the various methods is excellent. For example, McNeill and Green (23), using a NaI crystal spectrometer, have reported the average potassium concentration in a group of 30 Canadian male subjects 19 years of age to be 2.12 $\pm$ 0.04 g. K/Kg. Los Alamos Scientific

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Laboratory results (7), with the liquid scintillation counter for a group of 21 American subjects 19-20 years old, are 2.15 ± 0.05. MacGillivray and associates (19), using K^{42} dilution, found for 32 females (Scotland) aged 25-49 years an average value of 1.60 ± 0.04 versus the LASL value of 1.63 ± 0.02 for 176 subjects of this age group. Also using K^{42} dilution, Wayne and associates (32) found 1.98 ± 0.08 for 7 males (Scotland) aged 21-22 years, compared with the liquid scintillator value of 2.12 ± 0.04 for 37 American males aged 21-23 years. All errors given above are estimates of the standard error of the mean, calculated from the standard deviation of individuals from the group mean (10-14%) and the number of subjects measured. More detailed correlations with K^{42} data are discussed later. This excellent agreement of the potassium concentrations for specific age groups in different population samples indicates that an accurately reproducible parameter is being measured.

The purpose of the present paper is to analyze further the age dependence of potassium concentration and to attempt to eliminate the effects of variation in fat and skeletal mass through the use of body water determinations. Body water was chosen as the other parameter, since it shows an unusually good correlation (standard deviation only 2.1%) with the dehydrated defatted protoplasmic mass of the body, M_3 (2). M_3 is defined as the residual mass of the body after removal of bone mineral (m), fat (F), and water (W) from the gross body mass (M), i.e.,

$$M_3 = M - (m + F + W). \quad \text{(Eq. 1)}$$

For isolated tissue, this residual mass has a uniform density of $D_3 = 1.398$ g. ml.$^{-1}$ (1). The relationship holds even for bone, when corrected for the high density of dry bone mineral (3).

Independent of age and sex, the relationship between W and M_3 is a constant, δ (1, 2):

$$\delta = W/(W + M_3) = 0.784 \pm 0.0161 \quad \text{(Eq. 2)}$$

so that under the stated conditions as to health and abstinence from food for 12 hours,

$$M_3 = [(1/\delta) - 1]\ W = (0.276 \pm 0.0057)\ W \quad \text{(Eq. 3)}$$

This relationship is used in the present paper to evaluate M_3 from body water measurements for purposes of comparison with total body potassium determinations. In addition, a comparison of total body potassium with basal metabolic rate (BMR) is made.

MATERIALS AND METHODS

Measurements of the natural gamma radioactivity of the 1590 subjects reported by Anderson and Langham (7) were made with a large liquid scintillation counter described elsewhere (4, 6). The counter provided essentially 100% geometrical efficiency (4π steradian solid angle) for a counti - well 18 inches in diameter by 6 feet long . which the subjects were placed. By use of energy discrimination, only the gamma rays from K^{40} were counted. Three minutes of counting time per subject gave a statistical precision of ± 3 Gm. of potassium (standard deviation), or about 2% for the average adult male. The counter was calibrated with weighed quantities of KCl mixed with quantities of sucrose ranging from 80-200 pounds and also with known quantities of K^{42} ingested by persons of various weights. The precision of the counting method, as judged by internal consistency and reproducibility, was essentially the same as the counting statistical error (i.e., about 0.08 equivalent of potassium). The absolute accuracy of this method is harder to establish but seems to be better than 5%, as judged by comparison with other methods. The population sample was predominantly New Mexican, but no significant geographical effects were apparent in the primary data. Excellent quantitative agreement has since been obtained for a second U. S. population sample (33) and for a German population (25). The original sample consisted of all visitors to the Health Research Laboratory who volunteered for measurement.

Potassium and body water by HTO dilution were determined on an additional 38 subjects (10 being women) ranging in age from 16-51 years. For 19 of these subjects, body water was independently estimated from HDO dilution (2). The estimated precision of the water determinations was $\sigma = 0.67$ Kg. Unfortunately, it was not feasible to determine body water on the earlier group of 1590 subjects for whom total body potassium measurements were made. In using these data in the present study it is necessary, therefore, to make use of previously reported average values for body water as a function of age.

Basal metabolic rates (BMR's) were determined in 17 healthy male subjects 22-44 years

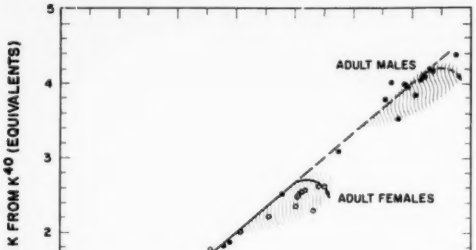

Fig. 1. Correlation between total body potassium (from K^{40} counting) of males and females of all ages and their M_3 mass derived from δ and average total body water.

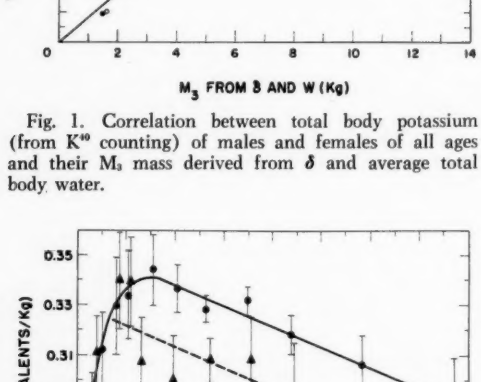

Fig. 2. Variation in the ratio of total body potassium to M_3 as a function of age and sex.

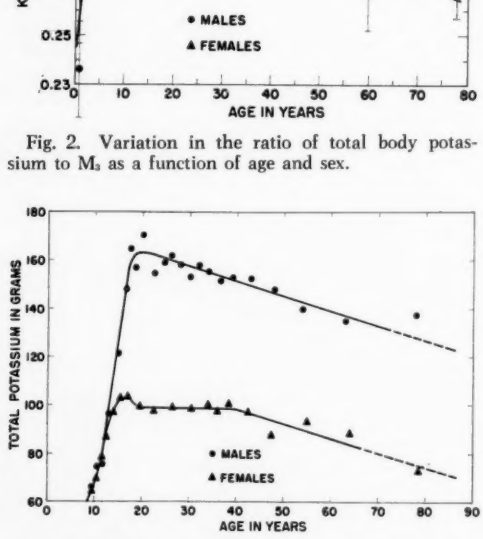

Fig. 3. Total body potassium content of males and females as a function of age.

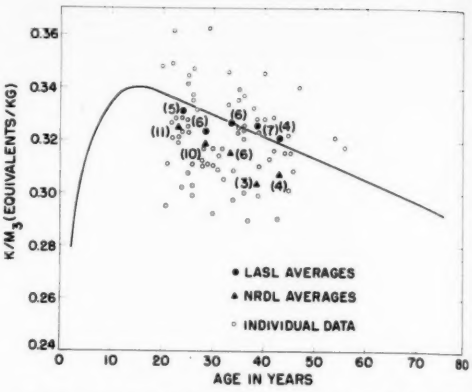

Fig. 4. Ratio of body potassium to M_3 of adult males for whom body water and potassium were determined simultaneously.

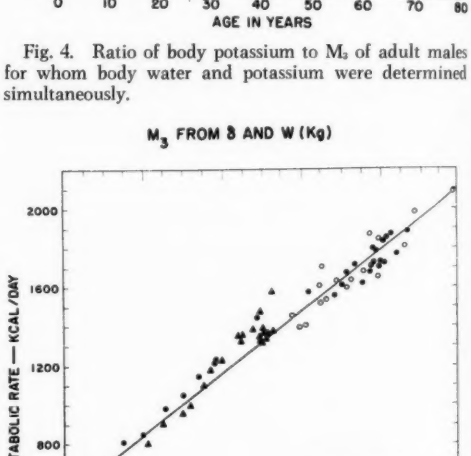
M3 FROM δ AND W (Kg)
BASIC METABOLIC RATE — KCAL/DAY
○ INDIVIDUAL MALES
• MALE AVERAGES
▲ FEMALE AVERAGES
TOTAL BODY POTASSIUM — EQUIVALENTS

Fig. 5. Comparison of total body potassium with basal metabolic rate.

of age within a few days of the determination of potassium. Three determinations were made of the average time required to consume 1 L. of pure oxygen while the subject was still in bed immediately after being wakened.* To calculate the BMR, a respiratory quotient of 0.82 was assumed, giving a caloric equivalent of 4.825 kcal. to 1 L. of oxygen (8). From this, the BMR was calculated in the units kcal. day^{-1}.

* These tests were performed by B. E. Welch and J. M.Iacono of the Nutrition Laboratory in the Los Almamos Medical Center.

TABLE 1. AVERAGE TOTAL BODY POTASSIUM CONTENT OF MALES AND FEMALES AS A FUNCTION OF AGE.

Age (Yr.)	Subjects (No.)	Average Weight (Kg.)	Average Weight S* (%)	Average Weight σ_m† (%)	Average Potassium Equiv.	Average Potassium S* (%)	Average Potassium σ_m† (%)
Males							
0	3	8.94	38.2	22.0	0.366	43.4	25.0
3	4	15.06	7.0	3.5	0.748	6.1	3.0
5	11	19.32	8.0	2.4	0.998	10.1	3.0
6- 7	24	24.64	16.3	3.3	1.282	15.4	3.1
8	85	27.54	15.7	1.7	1.505	11.4	1.2
9	59	31.92	18.7	2.4	1.703	13.6	1.8
10	54	35.33	21.4	2.9	1.909	15.5	2.1
11	18	36.51	15.3	3.6	1.929	10.6	2.5
12-13	26	47.69	18.0	3.5	2.456	12.6	2.5
14-15	27	54.95	23.3	4.5	3.099	9.0	1.7
16	16	62.64	18.7	4.7	3.786	7.3	1.8
17	17	71.68	16.0	3.9	4.207	9.9	2.4
18	10	69.09	14.7	4.6	4.013	10.1	3.2
19-20	21	79.26	17.9	3.9	4.358	11.3	2.5
21-23	37	72.75	14.8	2.4	3.956	10.8	1.8
24	24	76.87	17.7	3.6	4.081	13.2	2.7
25-26	28	78.25	13.5	2.5	4.143	12.8	2.4
27-28	56	76.08	13.8	1.8	4.043	13.2	1.8
29-30	77	73.50	15.3	1.7	3.912	12.7	1.4
31-32	52	79.66	15.2	2.1	4.034	10.8	1.5
33-34	79	77.35	14.2	1.6	3.990	11.2	1.3
35-37	84	75.25	14.7	1.6	3.872	12.1	1.3
38-39	43	78.51	10.2	1.6	3.905	10.7	1.6
40-45	88	78.64	14.0	1.5	3.900	10.6	1.1
46-49	34	78.33	12.4	2.1	3.684	7.7	1.3
50-57	46	75.15	14.0	2.1	3.575	9.8	1.4
58-68	30	76.32	12.4	2.3	3.445	10.9	2.0
70-85	4	81.59	10.4	5.2	3.520	12.7	6.3
Females							
0- 1	5	8.64	23.0	10.3	0.384	27.0	12.1
3- 4	5	15.54	15.7	7.0	0.808	22.3	10.0
5- 6	12	20.19	13.5	3.9	1.047	14.6	4.2
7	23	24.25	17.2	3.6	1.255	11.9	2.5
8	30	26.58	17.6	3.2	1.509	13.6	2.5
9	40	28.19	16.4	2.6	1.587	13.0	2.1
10	58	33.15	20.3	2.7	1.773	13.2	1.7
11	38	39.30	15.2	2.5	2.009	13.9	2.3
12	15	45.70	19.3	5.0	2.208	15.4	4.0
13-14	26	52.41	11.8	2.3	2.477	13.4	2.6
15	12	58.07	18.9	5.4	2.629	12.9	3.7
16-17	25	56.93	11.0	2.2	2.651	9.6	1.9
18-20	11	57.03	13.6	4.1	2.525	18.0	5.4
21-23	12	54.33	13.9	4.0	2.497	10.5	3.0
24-27	32	58.15	15.6	2.7	2.527	9.9	1.7
28-32	42	58.17	13.9	2.1	2.507	12.3	1.9
33-34	22	59.52	15.9	3.3	2.557	16.8	3.5
35-36	14	58.41	17.7	4.7	2.486	17.6	4.7
37-39	24	63.75	18.6	3.8	2.576	13.7	2.8
40-44	22	60.00	15.8	3.4	2.475	11.7	2.5
45-49	20	58.77	13.0	2.9	2.238	14.6	3.3
50-59	23	66.21	14.8	3.1	2.389	12.6	2.6
60-67	18	69.29	16.0	3.8	2.261	12.6	3.0
78-79	3	54.24	2.7	1.6	1.855	13.8	8.0

* Observed standard deviation from the average for the age group in %.
† Calculated standard error of the mean, $\sigma_m = \sigma/\sqrt{n}$.

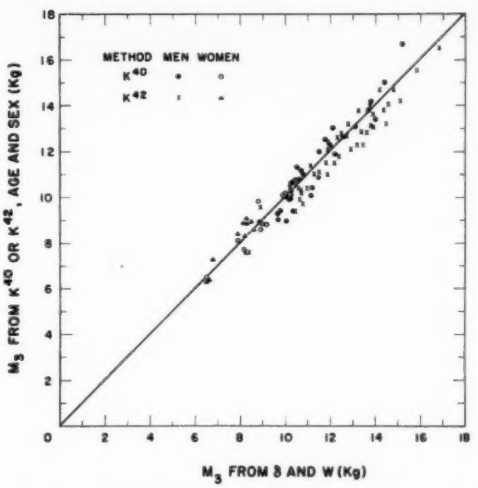

Fig. 6. Agreement between M_3 derived from K^{40} and K^{42} measurements (adjusted for age and sex) and M_3 derived from δ and total body water measurements.

RESULTS

Table 1 summarizes body potassium measurements on 1057 male and 532 female subjects in terms of the averages by age groups for both sexes. Number of subjects, average gross weight in kilograms, and average total potassium in equivalents are given. Shown also are the observed standard deviations of the individual values for each age group from the group mean and the standard error of the mean, σ_m, calculated on the assumption that $\sigma_m = s/\sqrt{n}$, where n is the number of subjects measured. Except for the extreme age groups, the estimated precision of the mean is from 1.5-5%.

Table 2 summarizes data from the literature on body water as a function of age (2, 9, 16, 22). The values of σ_m are again estimated by dividing the standard deviation of each age group average by the square root of the number of subjects in the group. The average body water values for adult males is defined rather precisely (2-4%), but the uncertainty in values for children and females is much larger, ranging up to 8% because of the small number of subjects for whom data are available. In the present analysis, therefore, principal emphasis is placed on the adult male results. A plot of the data in table 2 as percentage body water versus age gives curves from which percentage body water at intermediate ages may be obtained by interpolation. Smoothing of the data by this process probably decreases somewhat the standard error of the mean for any given age.

Table 3 gives the experimental data for the 38 subjects on whom simultaneous measurements of body water and potassium were made.

TABLE 2. AVERAGE TOTAL BODY WATER (IN FRACTION OF BODY WEIGHT) AS A FUNCTION OF AGE.

Age (Yr.)	Body Water*								
	Men			Children			Women		
	Subjects (No.)	W/M	σ_m † (%)	Subjects (No.)	W/M	σ_m † (%)	Subjects (No.)	W/M	σ_m † (%)
0–1				8	0.626	8.1			
1–5				7	0.588	4.9			
5–10				4	0.591	6.6			
10–14	6	0.576	5.3				6	0.561	5.7
14–18	5	0.636	4.1						
18–22	12	0.615	3.1				6	0.522	5.8
22–30	48	0.585	1.9				18	0.511	2.6
30–40	31	0.561	2.0				8	0.511	5.6
40–50	15	0.556	2.4				4	0.490	6.5
50–60	6	0.544	4.0				5	0.478	5.6
60–80	3	0.541	6.7				5	0.462	5.9
Total	126			19			52		

* Weighted averages from deuterium and tritium water dilution measurements reported in Refs. 2, 9, 16, 22.

† σ_m (standard error of the mean, %) $= \frac{s/\sqrt{\bar{x}}}{\sqrt{n}} \times 100$, where s = observed standard deviation of the population group from its mean, $\bar{x}$, and n = number of subjects.

Figure 1 shows the average total body potassium for various age groups (based on the data in table 1), plotted against the average M_3 for the age group estimated by Eq. 3 from the measured average weight (table 1) and the average body water graphically interpolated from the data in table 2. The number of subjects per point varied from 3-5 for very young children (small values of M_3 and K) and up to 50-250 for the adult groups. By plotting the ratio of K/M_3 in equivalents per kilogram as a function of age (fig. 2), deviations from the straight line of fig. 1 (corresponding to K/M_3 value of 0.332) can be emphasized.

In figure 2, the standard error of each point is indicated. This error is assumed to be due entirely to the uncertainty in the value of percentage body water as a function of age, as tabulated in table 1. Because of the much larger population groups available for K^{40} counting as compared with body water measurements, this seems to be the case. While (for adults) the decrease of K/M_3 with age and the sex difference are unmistakable, the scatter in the points is such that the slope is uncertain by $\pm$ 50%. This is particularly true for the female points, because of the small population sample for which body water data are available. These curves may be compared with those showing age and sex variation in total body potassium given in figure 3 and with the previously published ones showing age and sex dependence of potassium concentration expressed in Gm./Kg. of gross body weight (7). In the latter case, the results include changes in fat, connective tissue, and skeletal mass with age, while figure 3 also includes effects due to variations in total body mass.

The correlations shown in figure 2 are based on statistical treatment of population averages and on the assumption of the reality of certain correlations, specifically on the variation of average body water with age. One can, therefore, investigate whether the relationships indicated in figure 2 also apply to individuals for whom simultaneous measurements of both potassium and body water were made. Figure 4 shows the results of such a comparison. The curve is that deduced for males in figure 2. The open circles represent individual data on 72 adult males, 10 reported by McMurrey and associates (22), 28 collected at the Los Alamos Scientific Laboratory, and 34 reported by the Naval Radiological Defense Laboratory (9). The solid circles show averages for 5 age groups of the 28 subjects measured at LASL, and the solid triangles represent similar averages for the 34 subjects measured at the NRDL. In the latter subjects, the body potassium was measured by K^{42} isotope dilution after waiting 48 hours to ensure establishment of equilibrium.

Shown in figure 5 is the relationship between total body potassium and BMR. Open circles are the results for the 17 male subjects actually tested as to metabolic rate. The correlation coefficient is r = 0.896, and the equation of the least squares best fit to these data is BMR (kcal. day^{-1}) = 521 + 314 (K) (equiv.)

For the remaining 1590 subjects, the basic metabolic rates for specific age groups were calculated from the equations of Brody (10) using observed sex, age, and weight as parameters. The points for the large group show a linear correlation coefficient of r = 0.976 between BMR and K.

TABLE 3. SIMULTANEOUS DETERMINATIONS OF BODY WATER, POTASSIUM, AND M_3 IN 38 ADULT MALES AND FEMALES.

Subject	Age (Yrs.)	Total Body Water (Kg.)	Total Potassium (Equiv.)	M_3* (Kg.)
Males				
WCR	22	38.08	3.80	10.52
PN	23	50.68	4.49	14.00
AR	24	37.65	3.14	10.40
DWL	25	49.99	4.75	13.81
CEC	25	44.27	3.98	12.23
FK	26	40.40	3.34	11.16
HFG	26	52.02	4.99	14.37
BEW	28	37.28	3.32	10.30
ALF	28	37.07	3.27	10.24
GIB	29	55.02	5.50	15.20
WHS	30	36.42	2.94	10.06
JMI	31	41.12	3.57	11.36
RLS	32	40.58	3.24	11.21
JBS	33	43.44	4.00	12.00
KTW	33	42.72	4.09	11.80
VER	35	38.84	3.64	10.73
PSH	35	45.61	4.09	12.60
JFS	36	32.22	2.89	8.90
WRW	36	41.63	3.88	11.50
ECA	36	36.38	3.26	10.05
LJB	36	35.11	2.91	9.70
JFM	39	49.74	4.44	13.74
CCL	40	38.23	3.46	10.56
CEP	40	43.80	4.17	12.10
JEF	42	39.10	3.50	10.80
OSJ	42	35.15	3.07	9.71
THA	42	47.57	4.32	13.14
WHL	44	35.62	2.98	9.84
Females				
BR	16	23.53	1.88	6.50
GAT	27	37.43	3.07	10.34
VJB	29	31.86	2.86	8.80
CFB	29	32.36	2.50	8.94
PCS	31	35.87	2.94	9.91
JMW	31	33.23	2.56	8.94
BSR	34	28.60	2.36	7.90
CWC	35	32.62	2.55	9.01
IUB	40	29.58	2.19	8.17
EKH	51	36.20	2.82	10.00

* $M_3 = (0.276 \pm 0.0057)W$, where W is total body water.

For the adult female averages did not rise above an M_3 of about 9 Kg. and a total K of 2.6 equivalents and seemed to fall into the shaded area to the right and below the line extrapolated from the children's points. Male averages continued to rise to a maximum M_3 of 13.8 Kg. and K of 4.4 equivalents at age 20. The average point for 13-year-old males corresponds approximately to the average for adult females. Adult male points scatter away from the line into the shaded area in a manner similar to that shown by the adult female averages.

DISCUSSION

Figure 1 shows that a crude but direct relationship exists between total body potassium of growing males and females and their fat-free dehydrated protoplasmic mass (M_3), when the latter is derived from average body water in accordance with Eq. 3. Disparities in the relationship seem to appear in the adult age groups of both sexes. Up to age 11-12, corresponding to an M_3 of about 6 Kg., there was no apparent significant sex difference, and K increased approximately linearly with M_3. The adult female averages did not rise above an M_3 of about 9 Kg. and a total K of 2.6 equivalents and seemed to fall into the shaded area to the right and below the line extrapolated from the children's points. Male averages continued to rise to a maximum M_3 of 13.8 Kg. and K of 4.4 equivalents at age 20. The average point for 13-year-old males corresponds approximately to the average for adult females. Adult male points scatter away from the line into the shaded area in a manner similar to that shown by the adult female averages.

The deviations from the approximately linear relationship indicated by figure 1 are emphasized in figure 2, which shows the variation in K/M_3 with age. Although the scatter in points is such that the slopes of the lines representing the relationships between K/M_3 and age are uncertain by $\pm 50\%$, sex and age differences are unmistakable and the change in body potassium concentration with age persists even after correction for mass of fat and bone min-

TABLE 4. AGREEMENT BETWEEN M_3 DERIVED FROM TOTAL POTASSIUM (CORRECTED FOR AGE AND SEX) AND M_3 DERIVED FROM δ AND TOTAL BODY WATER.

Method	Males			Females			Reference
	(No.)	$\bar{d}$ (%)	σ_d (%)	(No.)	$\bar{d}$ (%)	σ_d (%)	
K^{40}	28	+0.06	5.58	10	−2.82	4.97	Present
K^{42}	35	−2.88	4.31	..	.....	....	(9)
K^{42}	10	+0.41	4.46	10	+0.08	4.71	(16)

eral. The latter conclusion is supported further by the results in figure 4, showing individual values and age group averages for K/M_3 derived from body water and potassium measurements on the same individuals. These data were collected in three different laboratories in which body potassium was determined by two different methods. Although the individual points scatter widely, agreement between the age group averages and the statistically derived curve is strikingly good, despite the small number of determinations in each group. The average ratio of K/M_3 values by isotope dilution and by whole body counting is 0.967. The 3% discrepancy may be due to a consistent calibration error or may represent the fraction of nonexchangeable potassium, or both.

The age effect for both sexes seems to be due more to a slight loss of body potassium as noted by Sievert (29) and Sagild (27) than to an increase in M_3. The rate of change of body potassium of adult males with age is reduced from 0.42%/year, when total potassium is considered (fig. 3), to 0.25%/year, when potassium is related to M_3. The scatter of individual points about the averaged curve is reduced from $\sigma = 12\%$ to $\sigma = 5\%$. The standard deviation of the individual potassium values about the average for their age group corresponds to an age effect of 30 years in the former case and 20 years in the latter. The use of combined potassium and body water determinations, therefore, does not enhance the precision of the correlation sufficiently to make it a practical empirical method of estimating physiologic age of individuals. As a possible method of quantifying the aging process in population groups, the method seems to be worthy of further study. The determination of potassium alone by whole body counting of a group of 36 subjects would define the mean potassium content of the group to $\pm 2\%$, corresponding to a 5-year uncertainty in age.

Further experimentation is necessary to establish the physiologic basis for the change in K/M_3 with age. Any change in body composition affecting the relative amounts of potassium and water would be effective. Since potassium is predominantly intracellular, it may be taken as indicative of the amount of living cellular material; whereas M_3 (as derived from body water) is proportional to the total dry fat-free mass of the organism, excluding bone mineral but including other inert structural material and connective tissue. Connective tissue and other structural material may show a normal degree of hydration, but contain little or no potassium; in which case, its slow accumulation among the cells could produce the observed effect. A somewhat similar concept has been formulated by Sobel and associates (30) as the basis of their proposed hexosamine-collagen method of determining biochemical age.

An alternative possibility is that the changes seen in K/M_3 with age might be simply the result of changes in the ratio of the muscle mass to the mass of the other soft tissue. According to the data of Forbes and Lewis (17) on the potassium, water, and fat contents of the components of two dissected cadavers, the K/M_3 value for muscle is 0.331 equivalent/Kg., while the average value for all other soft tissue is 0.237. (Note that M_3 here is determined experimentally and not calculated from water content.) Assuming that K/M_3 is invariant with age and that these values are typical, one can calculate the average K/M_3 for the body as a function of fractional muscle mass. If the fraction of body M_3 contained in muscle is x and the fraction in soft tissue is (1-x), then using the above values of K/M_3 for these two components, one finds for the entire body:

$$K/M_3 = 0.094x + 0.237 \quad \text{(Eq. 4)}$$

This equation gives K/M_3 values which are 6% low compared with the value from figure 2 for age 53, the average age of Forbes and Lewis' subjects. Assuming this to be due to a consistent calibration difference or to a deviation of these subjects from the normal population curve, Eq. 4 can be normalized to

$$K/M_3 = 0.100x + 0.252 \quad \text{(Eq. 5)}$$

On the basis of Eq. 5, one can calculate the changes in body composition necessary to account for the adult age variation of K/M_3 with age (fig. 2) on the assumption that the entire effect is due solely to a change in the ratio of the M_3 mass in muscle to the M_3 mass in other soft tissues. The result is that the fraction of M_3 represented by muscle would change from 84% at age 20 to 36% at age 80. The former fraction seems rather high, and the situation is even worse when individual males lying at 2σ (= 10%) above the average are considered. Muscle fraction now calculates to be 1.18 with no allowance at all for other soft tissue. Such individuals exceeding the calculated upper limit

of $K/M_3 = 0.352$ have been observed. A similar difficulty is encountered with the extrapolation to 80-year-old females lying 2σ below the average; here soft tissue calculates to 1.02 with zero muscle.

While the quantitative aspects of the above argument must not be taken too literally, the indication is that there is not sufficient difference in the average K/M_3 of muscle and soft tissue to account for the observed range of variation of this quantity. Therefore, another component with a much lower K/M_3 must accumulate, or alternatively the value of K/M_3 for individual tissue must vary, with age.

For estimation of gross body composition of individuals, total body counting gives results which are consistent with those obtained by K^{42} dilution (9) and, if correction is made for age and sex according to the curves of figure 2, with those obtained from body water measurements. The calculation of M_3 from total potassium for males beyond age 15 is based on the upper line in figure 2, the equation for which is

$$M_3 = K/(0.354 - 8.2 \times 10^{-4}\alpha) \quad \text{(Eq. 6)}$$

where M_3 is in Kg., K is in equivalents, and α is the chronological age in years. For females, the data are inadequate to define the curve precisely. As figure 3 clearly shows, the total potassium of women is extremely constant from age 18-40, so that the suggestion in figure 2 of constant potassium concentration over a similar age range may well be real. However, the large uncertainties in body water and hence in M_3 make it impossible to be sure of this at present. The lower (dashed) line in figure 2 is, therefore, drawn as a simple straight line without structure pending further study. The equation of this line is

$$M_3 = K/(0.33 - 8 \times 10^{-4}\alpha) \quad \text{(Eq. 7)}$$

analogous to that for males, but with a 6% lower intercept and with considerably greater uncertainty.

Figure 6 and table 4 compare values of M_3 derived from potassium determinations with those based on body water for the same individuals. The slope of the line fitted to the K^{40} and K^{42} data (9) by the method of least squares is not significantly different (at the 5% fiducial limit) from unity, and the intercept is not significantly different from zero. The regression equation of the combined data is:

$$M_3\,(K) = 1.007\,M_3\,(W) - 0.21$$

In addition to the constant relationship between W and M_3 (Eq. 3), it has been shown (2) that m/M_3, the ratio of bone mineral to M_3, is also constant and equal to 0.334. Since

$$F = M - (M_3 + W + m)$$
$$W = 3.63\,M_3$$
$$\text{and } m = 0.334\,M_3,$$

one can write F as a function only of M_3:

$$F = M - 4.964\,M_3,$$

permitting the direct estimation of body fat from M_3 as determined from body potassium.

Establishment of these correlations permits the use of the simple and rapid whole body counting method for body composition studies in healthy normal subjects instead of the more tedious isotopic dilution methods for potassium or water. The study of body composition in physiologically abnormal or diseased states (in which cases the basic assumption of constancy of such ratios as W/M_3 may not hold) will require specific evaluation of body density, body water, and bone mineral in addition to determination of potassium.

Measurement and interpretation of basal metabolic rates have had a long and somewhat involved scientific history (15). Our present interest is based on the assumption that a given active tissue mass might be characterized by a definite minimal metabolic rate, as well as by a definite potassium content. Data on the oxygen consumption of individual organs, as summarized by Drabkin (14), show that 4 organs (brain, heart, kidneys, and liver), which contain only about 8% of body potassium, are responsible for 70% of the BMR, whereas muscle with 60% body potassium contributes only 13-16% of the BMR. However, these crucial organs are functioning at a level determined by the requirements of the entire organism, and their metabolic level may be proportional to total cellular mass. [Krebs (18) has suggested that muscle metabolism may be the determining factor in the relationship between BMR and total body size for different animals.]

Our results indeed indicate a strong correlation between BMR and total body potassium (fig. 5), each equivalent of potassium being associated with a heat output of 314 kcal./day. This ratio seems to apply to both male and female adults and perhaps even to children, although greater experimental uncertainty in both quantities makes the latter conclusion less certain. It is less easy to understand the additional 521 kcal./day, which is apparently produced independent of body size and age. Fur-

ther study of the detailed structure of the data is indicated.

SUMMARY

Total body potassium, measured by gamma ray counting of the naturally occurring K^{40} isotope, provides a rapid and effective means of studying gross body composition. Total body potassium content is proportional to the body mass minus bone mineral, fat, and water (M_3) derived from the body water (W) according to the expression $M_3 = (0.276 \pm 0.0057)W$. During growth, both body potassium and M_3 increase linearly with age. In adulthood, M_3 and potassium appear to depend on both age and sex. The ratio of K/M_3 decreases with increasing age and is lower for females than for males. The physiological significance of decreasing K/M_3 with age is not apparent. It may indicate a basic change in cellular metabolism or a net loss in muscle mass with replacement by connective tissue having approximately the same degree of hydration. When corrected for age and sex, the correlation between M_3 derived from body potassium and body water is quite good, when body potassium is determined by either K^{40} counting or K^{42} dilution, and body potassium measurements provide a simple and rapid method of estimating body composition.

An interesting correlation is observed between total body potassium and basal metabolic rate, but further study is required to explain the detailed structure of this relationship.

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AN ATTEMPT TO QUANTIFY SOME CLINICAL CRITERIA OF AGING*

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Among the possible late effects of ionizing radiation exposure are shortening of life span and a process resembling premature aging. In animals these effects are evidenced by such changes as graying of the hair (7), appearance of degenerative changes in tissues and organs (1, 2), and deaths associated with degenerative diseases and malignancies (6). Although evidence for premature aging *per se* has not been observed in human beings, shortening of life span and increased incidence of malignancies have been reported in radiologists (10, 11). Japanese exposed to nuclear bombings have shown an increased incidence of leukemia (9). Another human population which received significant radiation exposure are the people of Rongelap Atoll in the Marshall Islands, who were accidentally exposed to fallout in 1954. In view of possible effects of radiation in producing premature aging, during the course of studies of these people it was desirable to develop a method of measurement of aging. It seems pertinent first to briefly summarize the radiation effects in the Rongelap people, since they were the subject of this study.

A group of 64 Rongelap people received an estimated 175 r of gamma radiation in addition to beta burns of the skin and some internal absorption of radionuclides. Also 18 other Rongelapese who, by virtue of being away on a nearby island, received only an estimated 69 r. Due to radioactive contamination of their home island, the people of Rongelap were moved to Majuro Atoll where they lived for the following three years. They returned to Rongelap in the summer of 1957 accompanied by some 100 unexposed Marshallese relatives who had not been living on the island at the time of the accident. This group served as an excellent comparison population. Both groups have been carefully studied at intervals for signs of radiation effects. The acute damage (such as hemopoetic depression, and skin burns) which have been described in previous publications (3, 4, 5) has largely subsided, and greater emphasis is now being placed on detection of late effects of radiation. Shortening of life span has not been apparent thus far. Four deaths have occurred: one in a 46-year-old man during the second year after exposure from hypertensive heart disease, which had been present at the time of exposure; the second in a 76-year-old man at three years post-exposure of coronary heart disease complicating diabetes of long standing; the third in a 36-year-old man 4 years after exposure with acute varicella; and the fourth in a 61-year-old female at 5 years after exposure of ovarian cancer. None of these deaths seemed to be directly related to radiation effect, and the incidence of mortality is about the same as for the Marshall Islands as a whole. No case of leukemia or cancer, except the one case of cancer referred to above, have occurred. The incidence of degenerative diseases seems to be about the same in the exposed as in the unexposed group. Reproductive capacity does not seem to have been impaired in the exposed group. A slight increase in the number of miscarriages and stillbirths seems to have taken place in the exposed women but, due to lack of vital statistics, this cannot be properly evaluated. There also was suggestive evidence of a slight lag in growth and development of exposed children during the first few years post-exposure, but this is being re-evaluated based on better age data. No genetic effects have been observed in the children born of exposed parents.

Although there has been no outward evidence by gross observation of any accelerated aging effect of radiation on the exposed group, it was believed that it would be desirable to have measured criteria of possible age changes that might occur on normal physical examination. Therefore the over-all objective of this study was to establish a series of tests to evaluate any possible radiation-induced senescence in the exposed group compared with the unexposed population living on the same island. However, a study of the data to be presented that was collected during the past survey (March, 1959) 5 years after exposure showed no apparent differences between the exposed and unexposed groups. Therefore the two groups have been pooled with the objective of

* This work was done under the auspices of the U. S. Atomic Energy Commission.

presenting the methodology of approach, the trend of changes for the various aging criteria chosen, and an attempt to determine a biological age score for the individuals and different age groups.

MATERIALS AND METHODS

This study was hampered by the small number of people involved and the lack of vital statistics on the Marshallese people. Another difficulty has been the uncertainty of exact ages in some cases, particularly in older people.

The aging criteria to be presented were recorded only in adults, that is in those 20 years of age and over. Data were recorded on 126 adults, 42 in the originally exposed group and 84 in the larger comparison population. Table 1 shows age and sex distribution of the people

TABLE 1. RONGELAP ADULT POPULATION AGE DISTRIBUTION (1959).

Age	Exposed		Unexposed		Total
	M	*F*	*M*	*F*	
20 - 24	0	5	1	6	12
25 - 29	2	1	12	6	21
30 - 34	3	2	3	5	13
35 - 39	1	4	4	4	13
40 - 44	4	2	6	3	15
45 - 49	1	0	2	3	6
50 - 54	1	0	5	5	11
55 - 59	2	1	3	1	7
60 - 64	0	6	5	3	14
65 - 69	0	0	2	3	5
70 - 74	1	2	0	0	3
75 - 79	0	1	0	0	1
>80	2	1	2	0	5
					126

examined. The ages were reasonably well distributed except for a smaller number of older people (> 60 years of age).

The age criteria chosen were based on changes generally believed to be associated with physiological senescence and represent only a small number of those that might have been considered. They were selected, however, with a view toward ease of assessment during routine physical examination under field conditions, time limitations, and language barrier. Therefore, unfortunately, tests of vigor and functional capacity were necessarily limited.*

There were 15 tests selected, 9 of which were measured directly and 6 of which were estimated on a 0 through 4+ scale. There were 5 tests involving the integument: 1) skin looseness, 2) skin elasticity (retraction time), 3) senile changes in the skin, 4) graying of the hair, and 5) baldness. There were four tests involving the special sense organs: 1) accommodation, 2) visual acuity, 3) arcus senilis, and 4) hearing. The cardiovascular system was tested by: 1) systolic and diastolic blood pressure recordings, 2) peripheral arteriosclerosis, and 3) retinal arteriosclerosis. There was one test of neuromuscular function. Vigor was measured by hand strength measurements. The methods used in carrying out these tests follow.

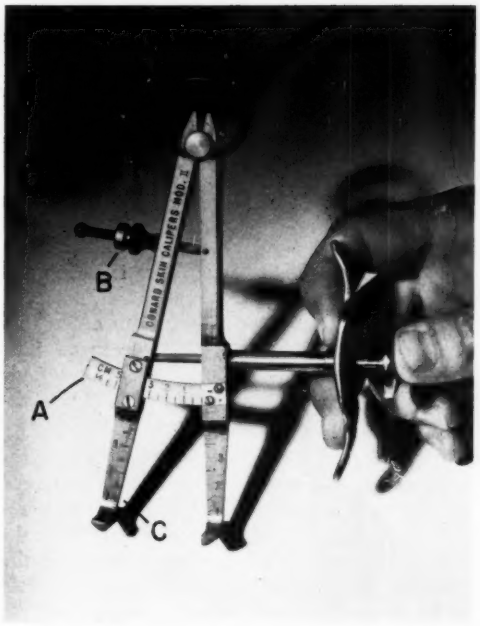


Fig. 1. Calipers used for measurement of skin looseness and elasticity.

Integument: A special skin caliper was designed for measuring skin looseness and elasticity. (See fig. 1.) The legs of the caliper can be opened to any desired degree to as much as 5 cm. (on scale "A" by adjusting screw "B" in fig. 1). The spring tension when the caliper is closed on a fold of skin results in a pressure of about 500 Gm. The inner and outer surfaces of the legs of the calipers are calibrated in millimeter markings ("C" in fig. 1).

1. *Skin looseness.*—Preliminary investigation revealed that the skin fold at the junction of the chin and neck was the most satisfactory for the measurement of skin looseness and seemed to be best correlated with age. The measure-

* There were several tests such as pulse-blood pressure response to a two-step test and vital capacity that were tried out but not used since they proved unsatisfactory.

ment of skin looseness was carried out by grasping the skin with the thumb and forefinger, pulling it gently outward, and applying the caliper opened to 4 cm. so that each leg was firmly against the skin lateral to the fingers. The caliper was then allowed to close by its own spring tension and the height of the fold of skin impinged was measured in millimeters on the scale "C" of the caliper. The elongated ends of the legs impinge on 1 cm.^{2} surface of skin and exert a pressure of 500 Gm. There is little variation in spring tension in the last 2 cm. closing range of the caliper. The height of the fold represented the degree of skin looseness. The presence of excess fat in the skin probably made the readings err on the low side, but it was not believed this resulted in serious error.

2. *Skin retraction time.*—The state of elasticity of the skin was found to be best measured on the back of the hand. The hand and forearm were placed at rest on the table. The caliper was opened to 2 cm. (as measured on the crossarm scale) and allowed to close on a fold of skin several centimeters proximal to the knuckles near the middle of the hand so that the long axis of the fold was diagonal (45°) to the longitudinal axis of the hand. (This was done to avoid natural folds of skin.) The caliper was allowed to remain closed for exactly 60 seconds, then removed and the time for the skin fold to retract back to the normal skin contour was measured in seconds. The exact endpoint was sometimes difficult to measure in older people, and if the fold had not retracted completely in 90 seconds, this time measurement was used.

A reliability test of the skin looseness and skin retraction time was run on 20 hospital patients of various ages. Measurements taken with the skin calipers were recorded by two examiners. The following mean values with their standard deviations were obtained: for skin looseness in millimeters, 20.85 ± 0.71 and 20.90 ± 0.70; for skin retraction time in seconds, 58.2 ± 8.13 and 58.75 ± 8.18. There was no significant difference between the means of the two examiners. Prior to the test, the two examiners ascertained that their techniques for using the calipers were alike.

3. *Senile changes in the skin.*—The exposed skin of the hands and face were observed for the presence of senile changes such as keratoses, nevi, and pigmentation. The degree of such change was estimated on a 0 – 4+ scale; only an occasional abnormality was scored as 1+, more abnormalities were scored ranging up to 4+.

4. *Graying of the hair.*—The degree of graying of the hair was expressed on a 0 – 4+ scale as follows: 0, no graying; 1+, slight "salt and pepper"; 2+, moderate "salt and pepper"; 3+, nearly complete graying; and 4+, complete graying.

5. *Baldness.*—The degree of baldness was expressed on a 0 – 4+ scale as follows: 0, no apparent balding; 1+, slight receding of the hair at the temples; 2+, marked receding of the hair at the temples with some thinning; 3+, marked thinning and baldness; and 4+, baldness complete to a monk's cap type.

6. *Special senses.*—(a) *Eyes.*

(1) *Accommodation.* — Accommodation was measured in diopters by use of the Prince refracting rule.* The average reading of the two eyes was used.

(2) *Visual acuity.*—Visual acuity was measured by Snellen's test.* It was found that by taking the square root of the average visual acuity (denominator) of the two eyes the scale was more compressed and more linear. Thus the best vision of 20/10 was represented at 3.2 (the square root of 10), the worst reading of 20/200 was represented as 14.1 (the square root of 200), and intermediate readings similarly recorded.

(3) *Arcus senilis* was estimated in the 0 – 4+ scale. Only slight limbic clouding was considered 1+ with increasing clouding to marked clouding as 4+.

(b) *Hearing.** — Audiometric examination was carried out in a tent in a quiet location. A rugged screening type audiometer was used.† Impairment of hearing was averaged for the two ears as follows: the decibel loss for each of 7 frequencies (200, 500, 1000, 2000, 3000, 4000, 7000) in each ear was averaged and a mean frequency loss in decibels for the two ears was obtained.

Cardiovascular changes:

1. *Blood pressure.* — Systolic and diastolic blood pressures were obtained with the stand-

* With regard to the reliability of determinations using the Prince refracting rule, Snellen's test, and hearing acuity, it should be pointed out that these tests were carried out under standardized conditions, but in view of the necessity of using an interpreter under field conditions, it was not feasible to repeat the test by more than one examiner. It is believed, however, that the data from these tests were sufficiently reproducible to be of relative value, although not so accurate perhaps as might be obtained under more desirable conditions.

† The author is grateful to the Armed Services Medical Procurement Agency, Fort Totten, N. Y. for loan of the audiometer.

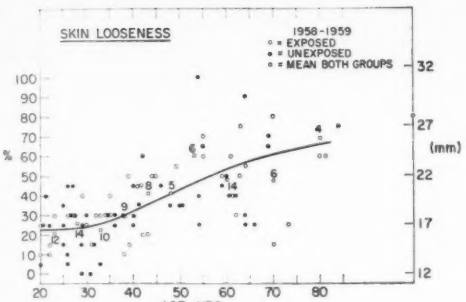


Figure 2.

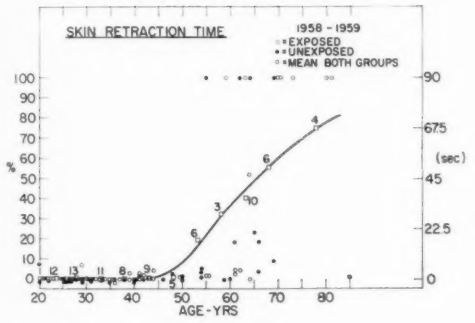
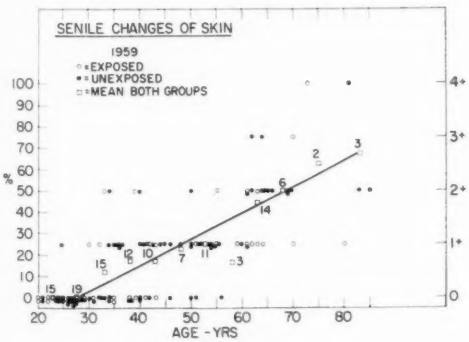


Figure 3.



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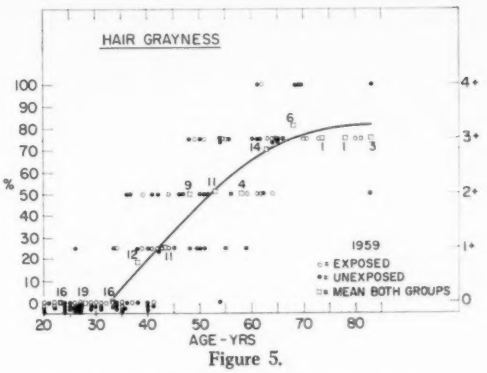


Figure 5.

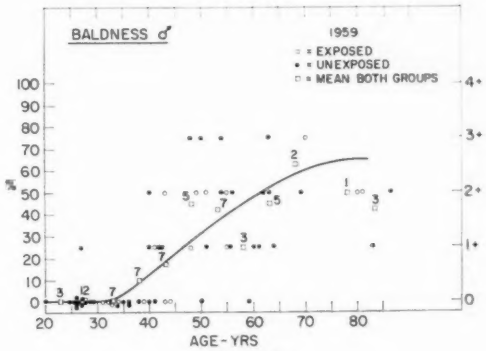


Figure 6.

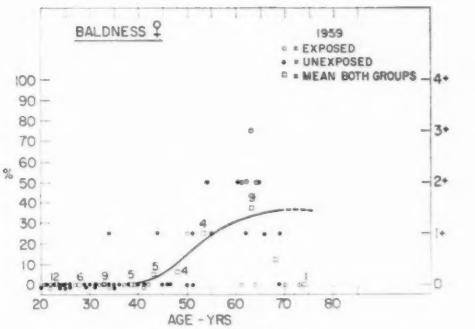
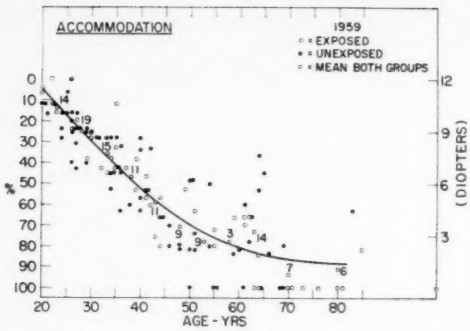


Figure 7.

ard aeronoid cuff type sphygmomanometer. Two readings were obtained and the average of the two was used. There was no basic or adjusted level of physical activity such as resting for a standard period prior to the readings. Pressures were taken from the left arm with the subject supine during the course of the physical examination.

2. The degrees of *peripheral arteriosclerosis* and *retinal arteriosclerosis* were estimated on a 0 – 4+ scale. Peripheral arteriosclerosis was estimated by palpation of peripheral arteries, retinal arteriosclerosis by viewing the retina with an opthalmoscope.

Neuromuscular function was measured by having the subject depress the key of a hand tally type of blood cell counter as many times as possible in the period of one minute. The total number of depressions represented the score.



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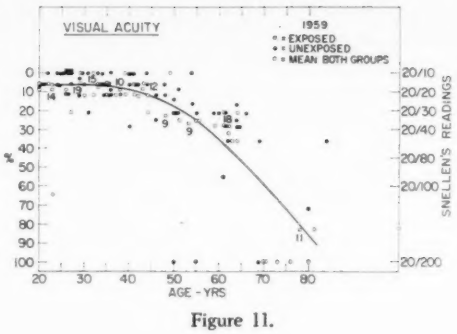

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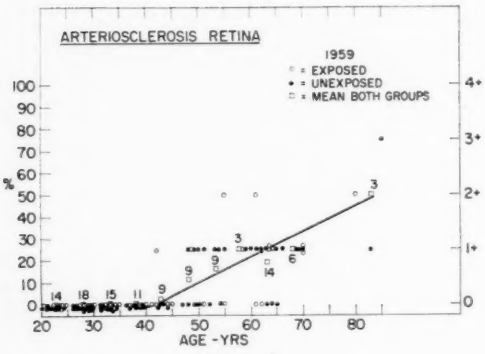

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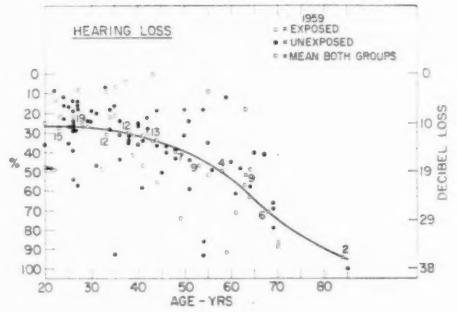

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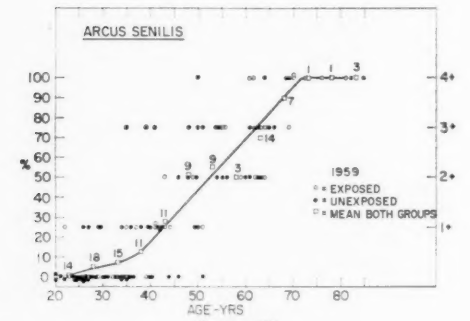


Figure 10.

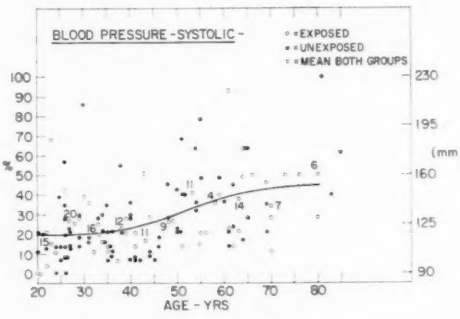


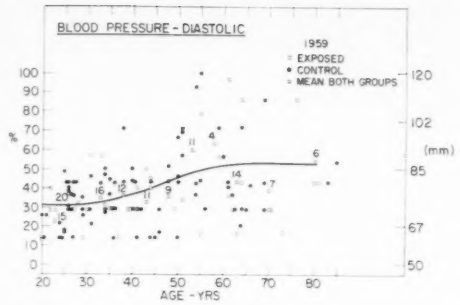
Figure 13.

Hand strength was measured by a Smedly hand dynamometer.* The spring tension of the hand grip was measured in kilograms. The maximum squeeze strength in the dominant hand in three tries was recorded.

Due to sex differences, the following criteria described above were evaluated separately for the two sexes: baldness, neuromuscular function, and hand strength.

* C. H. Stoelting Company, Chicago, Ill.

In order that the estimated and measured data could be compared and combined, both types of data were converted to a percentage scale. The estimated values of 0, 1+, 2+, 3+, and 4+ were thus presented also as 0, 25, 50, 75 and 100%, respectively. The measured data were similarly handled. Thus the values associated with least aging were chosen as 0% (sometimes the highest reading, as with hand strength; sometimes the lowest, as with hear-



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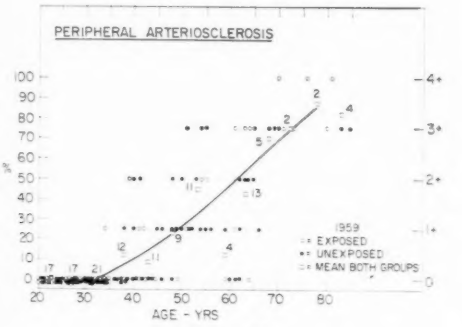

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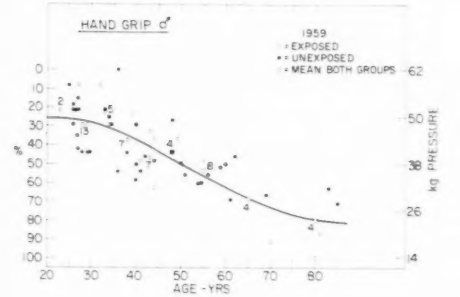

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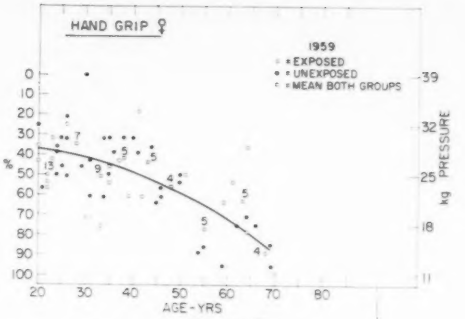

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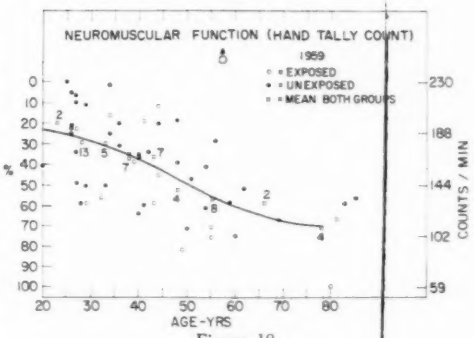

Figure 18.

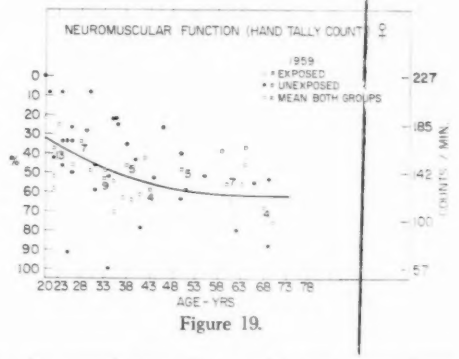

Figure 19.

ing loss), and conversely the values showing most aging were chosen as 100%. The data were examined on an individiual basis as well as on a population basis. A mean age score was obtained for each individual by averaging all the determinations in percentage for that individual. In studying population trends for the various criteria, mean points for 5-year age groups (in most cases) of combined exposed and unexposed populations were plotted and a best fit by eye curve drawn to show the trend of the data for the particular criterion. In the same way the average age scores were plotted for the population. By combining scores from individuals in each 5-year age group, it was believed that possible errors due to uncertainty of exact ages in some individuals were reduced

RESULTS

The results are plotted graphically in figures 2 through 20. Individual readings are plotted (open circles, exposed people; closed circles, unexposed people) to show the spread of the data and the mean values for each 5-year age group (squares). The trend of the various criteria with increasing age is represented by a best fit

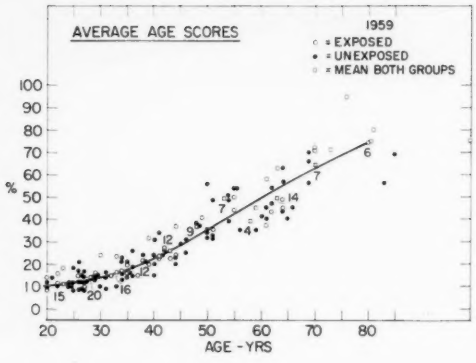

Figure 20.

by eye line. It can be seen that the criteria generally show either increasing or decreasing values with increasing age. Many of the changes, such as graying of the hair, balding, arteriosclerosis — peripheral and retinal, skin looseness, and skin retraction, do not manifest themselves appreciably until after ages 35 to 40 years in the Marshallese. There is a tendency in many of the curves for criteria, such as blood pressure, graying of the hair, and loss of visual acuity and accommodation to level off, plateau, or even show slightly reduced values in the older age group. The number of people in the older age group is too small to make this observation certain. However, American statistics on blood pressure (systolic and diastolic) do show a plateau effect beyond about 60 years of age and even a slight tendency to lowering of blood pressures beyond this age (8). By 65-70 years of age, arcus senilis in all Marshallese showed a 4+ change and so, of course, plateaued at a maximum. Some curves showed lower maximums than others. For example, baldness in women showed only 35% maximum, and arteriosclerosis of the retina showed only 45% maximum. It is likely that the difference in the maximums among the various criteria presented was due largely to differences in the degree of changes associated with the various criteria, but also probably due to the arbitrary nature of the scoring. The sex differences in hand strength and baldness were expected. In the neuromuscular function test slight muscle fatigue may have been a factor in causing the females to score lower, necessitating separate treatment.

DISCUSSION

The various changes generally associated with physiological senescence are known to show wide variability among individuals of the same age, and this was borne out by these data. However, some of the criteria seemed to be better indices of aging than others, based on the degree of change and the variability of the data observed.* Some of the better criteria seemed to be accommodation of the eyes, visual acuity, skin retraction, arcus senilis, graying of the hair, and hand strength. One would expect that the measured criteria would be more reliable than the estimated ones in view of the subjective element and less precise scoring of the latter. This seemed generally to be the case, although the estimated values for graying of the hair and arcus senilis were surprisingly well correlated with age. The amount of subcutaneous fat probably influenced the skin looseness measurements, but since loss of subcutaneous fat is somewhat age dependent, it probably influenced it in the right direction. In the future it is hoped that by statistical treatment of the data a weighting factor may be assigned to each criterion based on the degree of age-associated change and the degree of variability of the data. Since it is not always possible to run the complete battery of tests on each individual, use of such weighting factors on those tests run would tend to minimize disparity that might be related to the omission of tests that were not run.

The data presented must be considered as preliminary in nature and represent only a small fraction of the many varied changes that have been incriminated in the aging process. However, under the conditions of examinations of the Marshallese the battery of tests employed is necessarily limited. As more experience is gained, some of the tests may be eliminated and new ones added. It is believed the tests of vigor are extremely important in assessing aging and it is hoped that more tests of this nature may be added. At this time the data are presented to introduce a type of approach which might offer a feasible means of assaying biological age. Studies of the possible effects of radiation on the aging phenomenon in human beings may be aided by this method. In the case of the exposed Marshallese, results of further aging surveys will be carefully evaluated, comparing results in the exposed population with those

* Statement is not based on statistical analysis.

In the unexposed comparison population for differences which might indicate possible premature aging effects of radiation exposure. As pointed out, such differences have not been apparent thus far.

SUMMARY

In order to study possible premature aging effects of radiation in the people of Rongelap in the Marshall Islands, a series of measurable criteria generally associated with aging were recorded during the 1959 annual medical survey (5 year post-exposure) on 42 people who had been exposed to radiation and 84 unexposed Marshallese. The criteria were chosen on the basis of ease of assessment under field conditions considering time limitation and language barrier. Some criteria were assessed on observation by scoring on a 0 through 4+ and percentage basis (senile skin changes, graying of hair, baldness, arcus senilis, peripheral arteriosclerosis, retinal arteriosclerosis). The other criteria were measured directly and also expressed on a percentage basis (skin looseness, skin elasticity, accommodation of the eyes, visual acuity, hearing by audiometry, blood pressure, neuromuscular function, and hand strength). A skin caliper used for measuring skin looseness and elasticity was described. Since no differences were readily apparent between the exposed and unexposed people, the data were pooled and presented at this time to describe the methodology, trend of criteria changes with age, and attempt to assess biological age. Curves of the plotted data drawn by eye showed varying degrees of age-associated change with different criteria. The measured criteria were generally best correlated with age, particularly accommodation of the eyes, visual acuity, skin elasticity, and hand strength, although some of the observational criteria, such as arcus senilis and graying of the hair, seemed also to be fairly well correlated. A plot of the average percentage scores for individuals by age (biological age score) showed generally increasing scores with ages and less scatter than was noted with individual criteria. It is hoped that this approach may prove helpful in assessing aging in human beings and may offer a clue to possible radiation-induced aging.

The author wishes to express his gratitude to Mr. William Scott for his assistance in compiling the data; to Col. Austin Lowrey (MC) USA of Walter Reed Army Hospital, Drs. B. S. Blumberg of National Institutes of Health and W. H. Lewis of Memorial Hospital for their assistance in taking measurements on the Rongelap people.

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OBSERVATIONS ON THE FINE STRUCTURE OF OLD AGE PIGMENT*

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Two previous electron microscope studies of old age pigment in neurons resulted in essentially the same appearance and two distinct suggestions as to origin of these bodies. Hess (4) was of the opinion that the pigment particles might arise from mitochondria while Bondareff (1) thought they might be derived from or produced by the Golgi apparatus. The present work seems to bolster the opinion of Hess and in addition demonstrates certain ultrastructural characteristics of the pigment bodies.

MATERIALS AND METHODS

The observations recorded in this paper were made on dorsal root ganglia taken from a mouse 18 months of age. Ganglia from 6 other mice one year or more of age were also studied without adding or subtracting from the findings in the oldest and fortunately best fixed material. The mouse was decapitated and the ganglia were removed as rapidly as possible and placed in Dalton's (2) fixative for two hours. After fixation the ganglia were washed briefly in distilled water and carried from water to absolute alcohol by 10% stages. From absolute alcohol the material was transferred to a half and half mixture of alcohol and uncatalyzed plastic, then through three changes of pure plastic, and finally to catalyzed plastic of a syrupy consistency. The ganglia were embedded in No. 00 gelatin capsules and placed in a 45 C. oven for 24 hours. The plastic was a mixture of 15% methyl methacrylate in n-butyl methacrylate. Sections were cut with glass knives in a Porter-Blum microtome and photographed in an RCA EMU 3C microscope.

RESULTS

As shown in figures 1 and 2, dorsal root ganglion cells from aging animals contain small particles of high electron density. These bodies have the general size and distribution of mitochondria and, as illustrated by the two figures, their numbers vary greatly from cell to cell. Not illustrated is the fact that similar inclusions occur in the satellite cells, the capillary endothelium (6), and occasionally in myelinated axons as well as in the cell bodies of neurons.

At higher powers the pigment bodies display considerable diversity in shape, size, and internal detail. A common pattern is shown in figure 3. In this figure each body consists of at least three different parts. Most conspicuous are very dense subparticles situated mainly but not exclusively at the periphery of each mass of pigment. As shown in the inset figure, 3A, each of these parts displays a series of alternate dense and light bands in parallel array. The lines may be straight or curved and run in many directions within any pigment body. The general background material of each cluster is not greatly different from that of mitochondria in which the internal membranes are thickened and in disarray. Mitochondria of this type are numerous throughout the neurons and satellite cells in this material. A portion of one of them is depicted in the insert figure, 3B. In addition many of the bodies contain vesicles of less density, examples of these can be seen in figure 3 and also in figure 7.

Althought the densest portions of many of these complex bodies may appear amorphous, an ultrastructure of great precision appears in so many that it seems reasonable to consider that favorable fixation and sectioning would reveal such patterns in all of the very dense material. Other examples of the ultrastructure are illustrated by figures 4 and 6, where the patterns can be directly compared with a bit of myelin sheath, shown at the same magnification in figure 5. It is readily apparent from inspection of figures 5, 6, and 7 that the laminated portions of the pigment bodies show periodicities that are less than one-half that of myelin, and hence this material must be quite different in composition from myelin and presumably in mode of formation. Since both proteinaceous materials (8) and pure lipids (7) are known to assume a laminated ultrastructure of nearly equal periodicity, any interpretation of this portion of the pigment complex in these terms will not be attempted. Figures 7, 8, 9, 10, and 11 illustrate many of the various patterns exhibited by the pigment bodies. In

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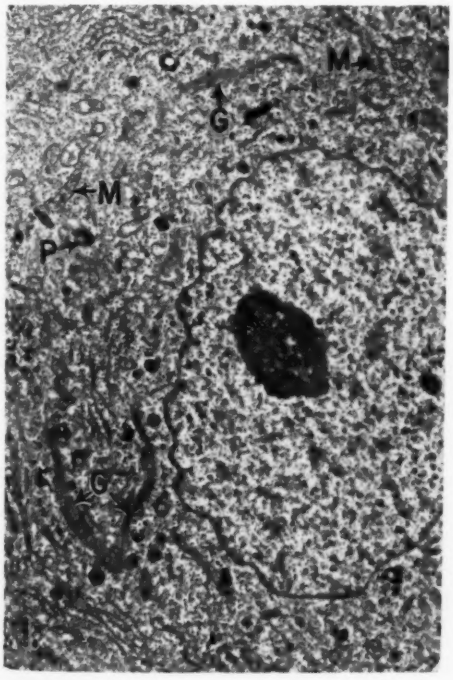
† Fellow in the USPHS experimental training grant No. 2R-29.

figure 7, double limiting membranes are discernible in many places and the interior of each body seems to contain strands of dense material which might be interpreted as thickened internal membranes of mitochondria. In figure 8 one body consists almost entirely of very dense amorphous material while the other one resembles the three nearby mitochondria. Figure 9 displays two distinct mitochondria, two pigment bodies, and one structure that could readily be accepted as a member of either category. The structures shown in figures 10 and 11 are quite common. They have double limiting membranes, which are identical to those of adjacent mitochondria, a matrix of more than the usual density for mitochondria in the same cell, and numerous vesicular profiles, which are thought to be disorganized internal membranes of mitochondria. The most striking feature of this variant of the pigment body is attached masses of dense material which display an ultrapattern and periodicity quite different from the dense material illustrated in figures 3, 5, and 7. The dense material seen in figure 7 may be the same as that shown in figure 11 but sectioned in such a manner as to exclude the double numbered body to which it is attached.

Fig. 12 shows three pigment masses that are attached to unequivocal mitochondria. While the pigment may be merely adherent, it blends with substance of the mitochondria without sign of intervening membranes or intervals. One could suggest that if these objects were the first mitochondria to be seen with the electron microscope the abnormal feature might well have been accepted as a characteristic of normal mitochondria at high magnifications.

In none of the material studied was there any close relationship of pigment bodies to the Golgi apparatus.



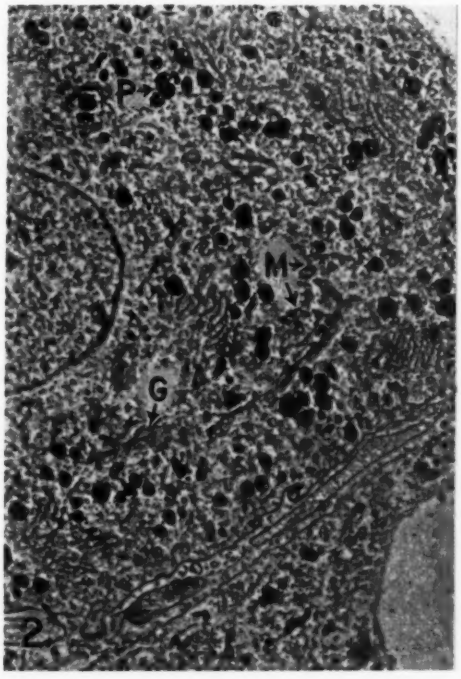


Fig. 1. Portion of a dorsal root ganglion cell showing pigment granules in minimal numbers: (M) mitochondria, (G) Golgi material, (P) Pigment. This and all other figures are from dorsal root ganglia of an 18-month-old mouse. X4,000.

Fig. 2. A portion of a dorsal root ganglion cell containing pigment granules (P) in abundance and close to the maximal seen in the material studied. Note that the granules have the general size and distribution of mitochondria (M) and no special relationship to Golgi material (G). X4,000.

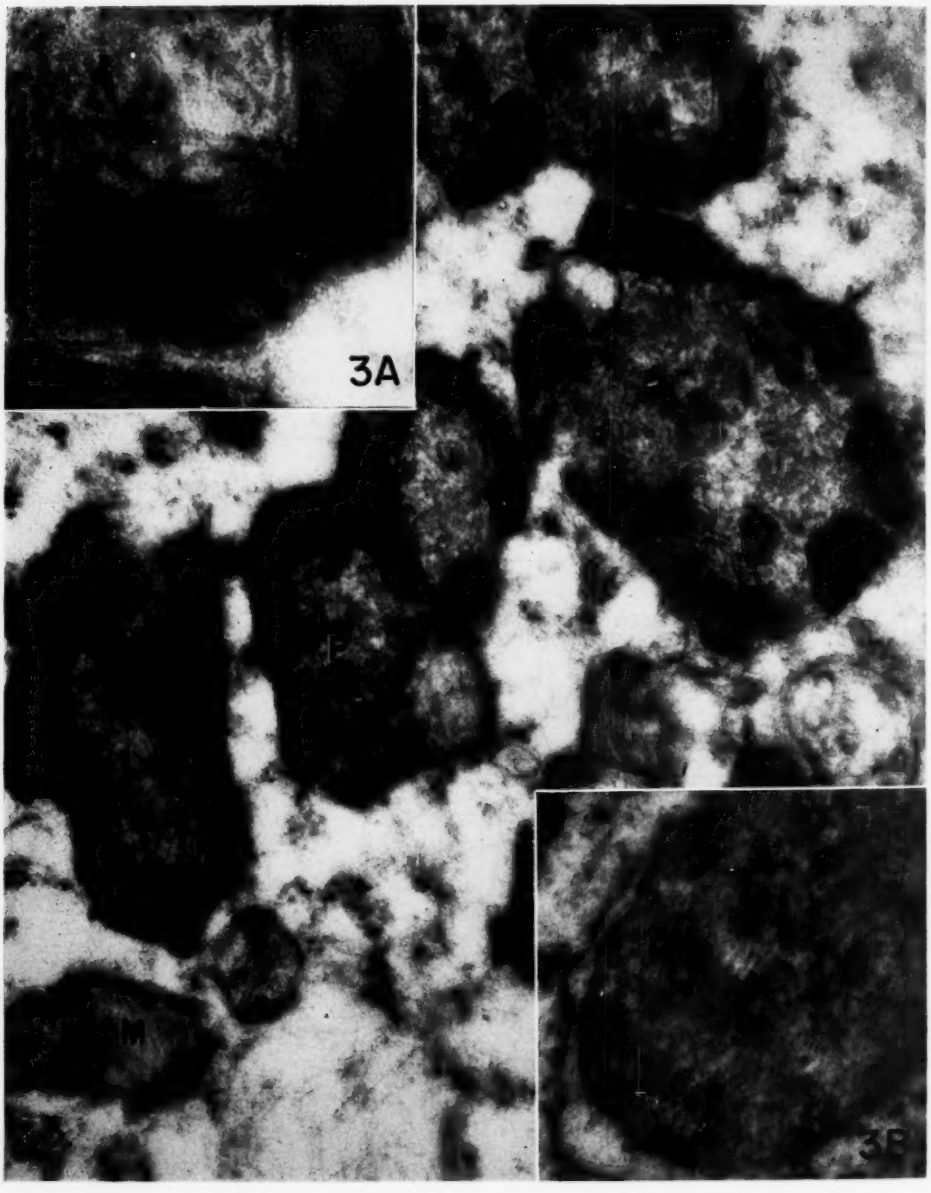


Fig. 3. To illustrate a common form of pigment granule (P). X45,000. Insert A (X110,000) is an enlargement of the granule to the right of the insert to show the laminated character of the densest components of the entire granule. Insert B (X45,000) is a portion of a very large and dense mitochondrion with disordered internal membranes. Note similarity of appearance between the interior of this mitochrondrion and that of the pigment granules.

Fig. 4. An example of the ultrastructural features of the dense material of the pigment granules. The narrower spacing is the most common and the wider may be an oblique section through the more closely spaced lines. X150,000.

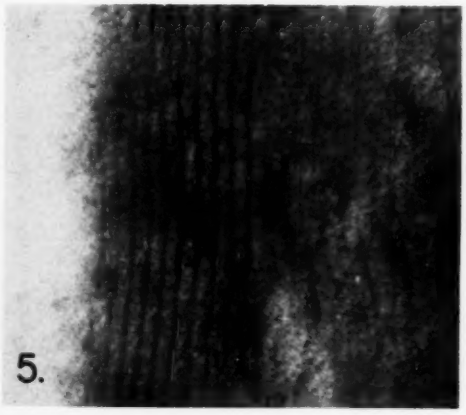


Fig. 5. A portion of a myelin sheath from the same material and at the same magnification. Note that the periods of true myelin are somewhat more than twice as wide as those of the dense material in pigment bodies. X150,000.

DISCUSSION

Since the complex bodies illustrated in this paper have been carefully identified as the material seen under the light microscope as lipofuscin or old-age pigment both by Hess and by Bondareff, no attempt has been made in this study to further correlate the two methods.

Unfortunately, electron microscope pictures are static and any interpretations involving

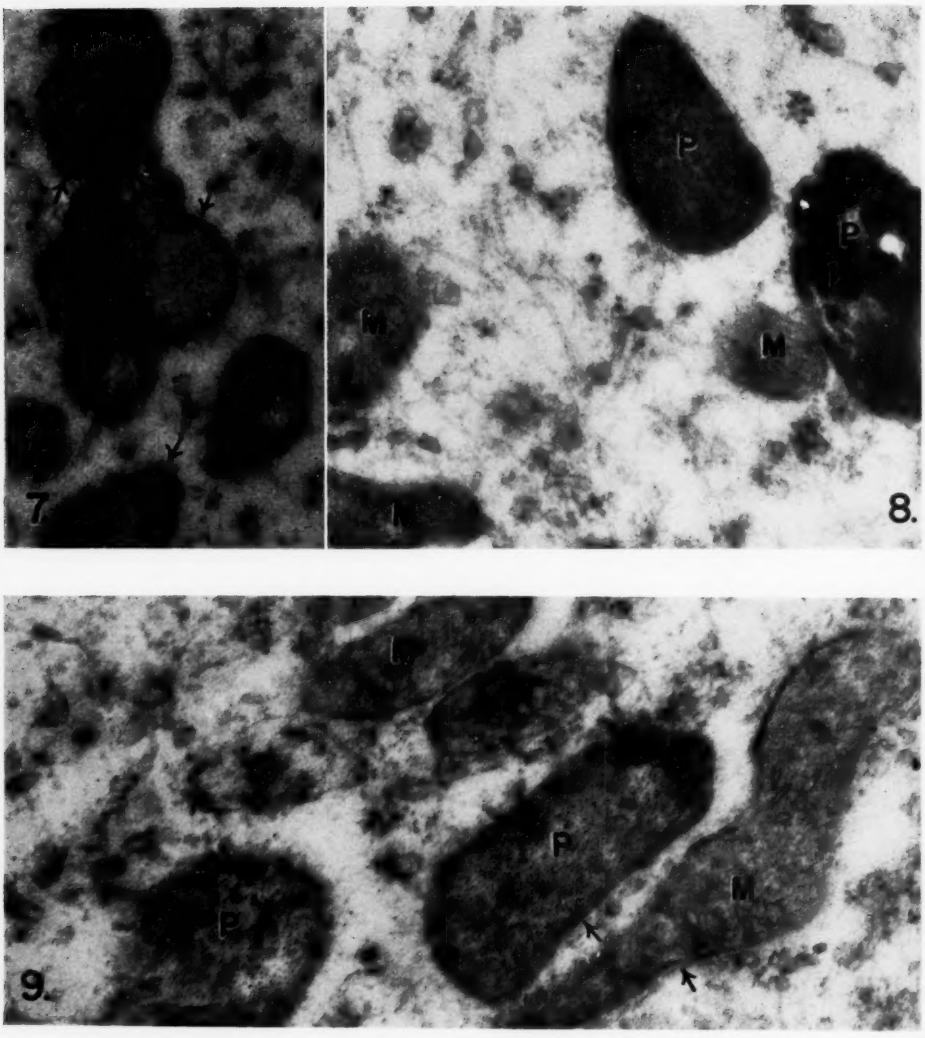
Fig. 6. A lattice pattern rarely seen in the present study. X150,000.

transformations must be advanced as suggestions rather than as an actual record of changes. Nonetheless, and with such limitations in mind, the most reasonable conclusion, based on the appearances, is that the old-age pigment arises as a process of alteration of mitochondria. Our pictures give no support to any other source.

One suspects that the varieties of form and the polymorphic interior of the pigment complexes have a significance in terms of chemical and physical properties that cannot be interpreted at present. Since mitochondria are notable labile structures, the well-established inertness of the old-age material should reside in the very dense substance which exhibits a highly ordered ultrastructure. There again one is confronted with the fact that many other substances organized in similar arrays such as myelin are exceedingly labile complexes.

At present there is little evidence on the extent to which the pigment bodies actually replace mitochondria in an uncompensated manner. Mere inspection of the material does suggest that cells heavily laden with pigment are correspondingly deficient in normal mitochondria. If this be so, such cells should have diminished powers of oxidation and in consequence a less active metabolism. However, there is much evidence against any appreciable change in function or metabolism resulting from pigment accumulation (5).

The old age pigment, as seen in this study, is remarkably similar to mitochondrial derived lipid bodies that accumulate in cultures of central nervous tissue from young animals (3).



Figs. 7, 8, 9 illustrate common, occasional, and rare forms of pigment bodies. Large numbers of the type shown in fig. 7 are present in the material studied, the type shown in fig. 8 is infrequent, and those depicted in fig. 9 are very few in number. Mitochondria are indicated by (M), pigment bodies (P), and places where double limiting membranes are most apparent are indicated by arrows. All figures X 45,000.

Fig. 10 shows a pigment body (P) and two mitochondria (M). Note that the matrix of the mitochondrion at the bottom of the figure and that of the main portion of the pigment body are virtually identical in appearance. X 45,000.

Fig. 11 depicts limiting membranes of a mitochondrion (M) and a pigment body (P) that are identical as to thickness, spacing, and density, see arrows. X 90,000.

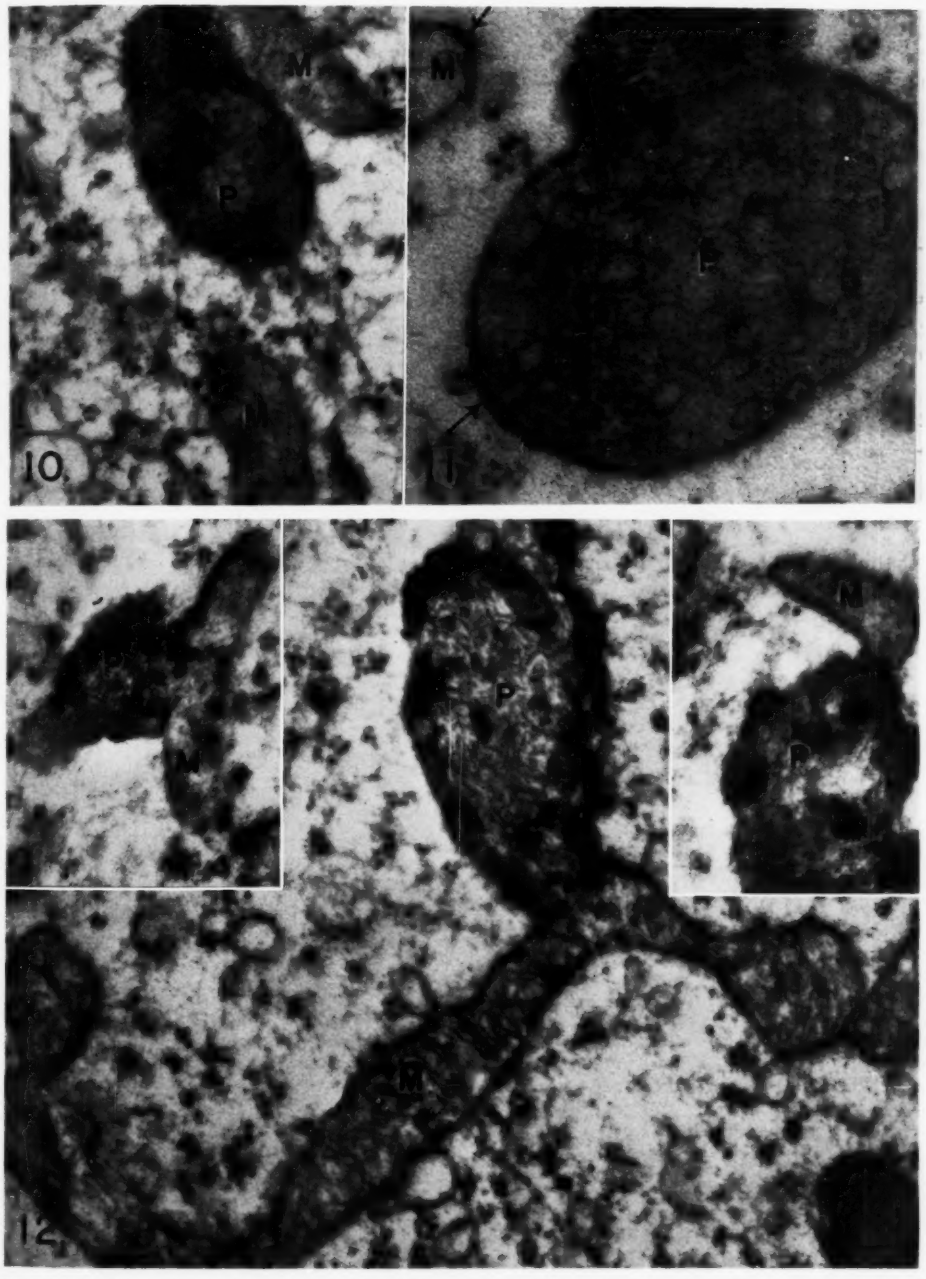


Fig. 12. This figure is a composite from three different plates to show direct continuation between typical mitochondria (M) and pigment bodies (P). The example in the upper right hand corner could readily be interpreted as a chance apposition, but the other two examples are highly indicative of the mitochondrial and pigment portions being part of a single composite body. X45,000.

This material, like the pigment, is acid-fast and highly resistant to solvents. If further work establishes the suspected identity of the old age pigment and lipid inclusions in cultured cells, the tissue culture may provide another method of greatly accelerating one of the most certainly established of old age changes at the cellular level, namely, the accumulation of an insoluble pigment.

SUMMARY

An electron microscope study of dorsal root ganglia from 6 mice over one year old revealed numerous complicated bodies of high electron density that are rare or missing in neurons of younger animals. These bodies may be attached to otherwise normal appearing mitochondria, or they may have features characteristic of mitochondria, such as double limiting membranes, internal dense bodies, and internal membranes. Many of the pigment masses contain lumps and clusters of very high density and a precise ultrastructure consisting of alternate light and dark lines in parallel array, sometimes straight, sometimes curved, and often running in several directions within a single body. It is suggested that this most dense material is the insoluble fraction of the pigment granule.

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SPONTANEOUS GLOMERULOSCLEROSIS IN AGING RF MICE

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Kidney lesions associated with senescence have been reviewed elsewhere (14). This study was undertaken to extend earlier observations on the incidence of spontaneous glomerulosclerosis in mice of the RF strain and to determine the earliest age at which such lesions could be observed histologically and their progression with time.

MATERIALS AND METHOD

Two hundred and twelve mice of the RF/Up strain (102 males, 110 females) were killed with ether at various ages from 1 to 20 months. Sections of kidney were placed in Halmi's fixative (9 parts SUSA: 1 part saturated aqueous solution of picric acid) overnight and embedded in Tissue-Mat at 56-58 C. by means of the Technicon procedure. Sections 5μ thick were stained with Harris's hematoxylin and eosin and studied for pathological changes. The following system was used for scoring the degree of change: Specimens exhibiting no apparent glomerular changes on comparison with the 4-week-old controls were classified negative (fig. 1); those with slight but definite hyaline change and thickening of the capillary wall of the glomerulus (fig. 2) were scored grade +; indefinite changes were classified as grade ±; grade ++ designated moderately severe hyaline change, in which approximately one-half of the glomerular tuft was affected (fig. 3); and more severely hyalinized glomeruli (fig. 4) were scored grade +++. In the latter category, over 75% of glomeruli showed almost complete hyalinization (fig. 5). To facilitate comparison of various grades of abnormality, a value of 1.0 was given to grade ± lesions; 2.0 to grade + lesions; 4.0 and 6.0 to grades ++ and +++ lesions, respectively. The absence of changes was scored as zero.

RESULTS

Moderate to severe glomerulosclerosis was usually present in animals 8 to 12 months old. Although inconsistently present before 6 months, the lesion seemed to increase in frequency and severity with age from 1 to 12 months (figs. 6, 7). After 12 months, however, there was no significant progression, and glomeruli of males 20 months old were only moderately affected. With increase in the severity of glomerular abnormality, size of glomeruli also increased (measurements of normal and damaged glomeruli, along with further details of the histopathologic changes, will be reported elsewhere). The renal tubules showed no significant abnormalities except for atrophy and dilation associated with severe glomerulosclerosis.

DISCUSSION

Spontaneous nephrosclerosis has been reported in aging rats (1, 12). Spontaneous intercapillary glomerulosclerosis has also been observed in aging mice, hamsters, and rats (9). Although similar lesions have been noted in irradiated rats (2, 3) and mice (5, 7, 9, 10), they occur in less than 5% of nonirradiated control LAF_1 [$(C57L \times A)F_1$] mice and in not more than 10% of those exposed to fractionated doses of radiation (4).

Renal lesions other than nephrosclerosis have also been observed in senescent animals. Spontaneous glomerulonephritis and nephrosis have been found in aging Sprague-Dawley rats (15) and in female mice of the NH strain (11). Glomerular lesions similar to those presented herein were described by Gorer (8) and subsequently likened to the changes of renal amyloidosis (6). Spontaneous renal amyloidosis was seen in strain A mice 8 to 12 months of age, reaching an incidence of 54% in older A mice (12 to 16 months) and 70% in old hybrid ABC mice (18 to 21 months) (6). Renal changes without amyloid were very rare in such animals. Lesher and associates (13) noted amyloidosis in LAF_1 mice receiving daily exposure doses of gamma radiation (6 to 12 r per day) as young as 15 months of age; nonirradiated mice developed the disease later, the peak incidence occurring at around 19 to 22 months. The age distribution of amyloid lesions in the LAF_1 mice simulates that of the glomerular changes reported herein. Thung

* Operated by Union Carbide Corporation for the U. S. Atomic Energy Commission.
We wish to acknowledge the assistance of Dr. A. W. Kimball in statistical analysis of the data and the technical assistance of Mr. Tennyson Mack and Mrs. Margaret Bradley.

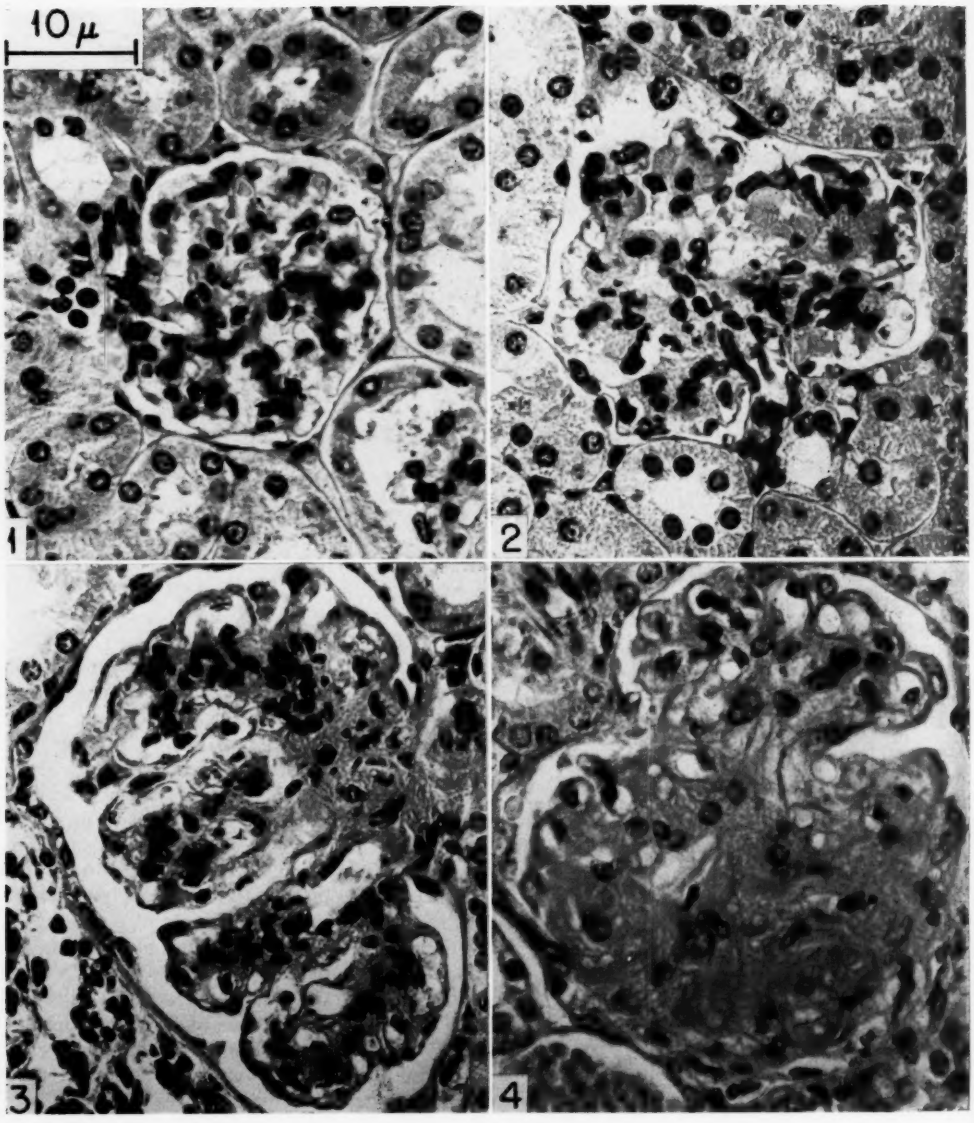

Fig. 1. Normal glomerulus, female RF mouse, H & E.

Fig. 2. Glomerulus showing thickened capiliary basement membrane (grade + lesion) H & E.

Fig. 3. Focal hyalinization of glomerulus (grade ++ lesion) H & E.

Fig. 4. Advanced hyalinization of glomerulus (grade +++ lesion) H & E.

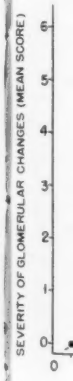

Fig. 6.
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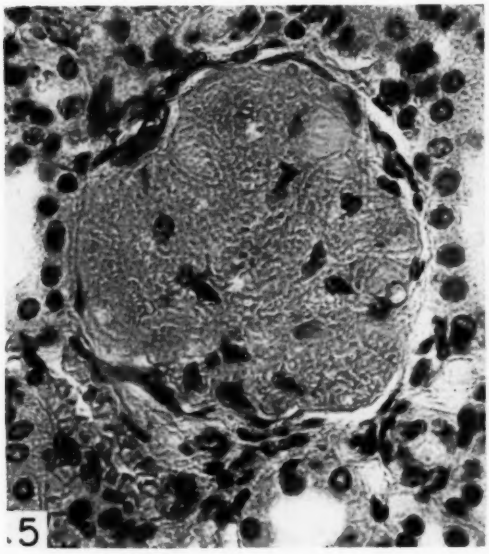

Fig. 5. Completely hyalinized glomerulus (grade +++ lesion) H & E.

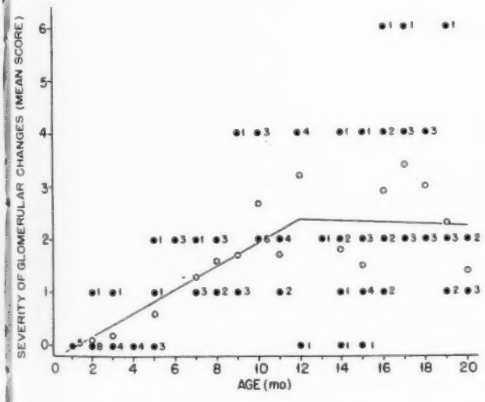

Fig. 6. Glomerulosclerosis in relation to age in female RF mice. (Number of animals at each point is indicated. Open circles represent the mean.)

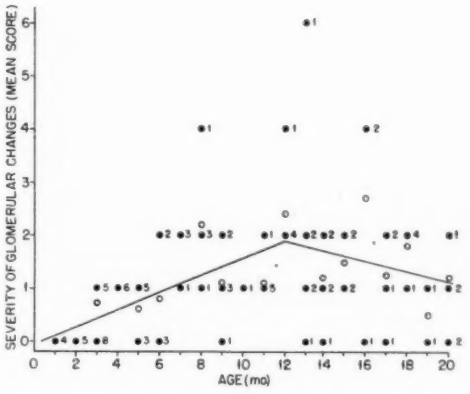

Fig. 7. Glomerulosclerosis in relation to age in male RF mice. (Number of animals at each point is indicated. Open circles represent the mean.)

(16, 17) has reviewed other observations on renal amyloidosis and related changes in aging mice.

In view of the foregoing, it is noteworthy that formalin-fixed, frozen sections of kidney and other tissues from the nephrosclerotic RF mice of this study were negative for amyloid when stained with crystal violet, congo red, and iodine. Preliminary data suggest that the spontaneous lesion reported herein resembles to some extent the spontaneous glomerular lesions reported by Guttman and Kohn (9) and the nephrosclerosis induced by irradiation in mice (4, 5, 7, 9, 10). From preliminary results, it is also evident that irradiation accentuates and hastens onset of the lesion. The pathogenesis of the disease and its possible relation to amyloidosis remain, however, to be elucidated.

SUMMARY

Aging male (103) and female (109) mice of the RF strain show spontaneous hyaline degeneration of renal glomeruli.

Glomerular changes are first consistently detectable in mice about 6 months old and increase in frequency and severity up to the twelfth month of age.

No definite relation between this lesion and renal amyloidosis is evident.

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AUTORADIOGRAPHIC STUDIES OF CHANGES IN S^{35}-SULFATE UPTAKE BY THE FEMORAL EPIPHYSES DURING AGING*

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Dziewiatkowski (7, 9) and Boström and Odeblad (5) revealed the incorporation of $S^{35}O_4$ in cartilage. The S^{35}-labeled compound in tissue was isolated (4, 8) and found to be essentially chrondoitin sulfate. Studies of $S^{35}O_4$ distribution and localization at the femoral epiphyses of 15-day-old rats were made by Dziewaitkowski (7, 9). It seemed that $S^{35}O_4$ uptake was highest at the proliferative and hypertrophic zones of the epiphyseal disk. Bélanger (1, 2, 3) followed the uptake of $S^{35}O_4$ in young rats and hamsters to 8 days after administration of the isotope. Apparently, shortly after administration of the isotope, the radiosulfate appeared within cells of the epiphyseal disk. Within one to two days, an increasing proportion of radioactive isotope was seen outside of the cells, and by 6 to 18 days the labeled sulfur was entirely extracellular. At this time newly-formed bony spicules exhibited greater radioactivity than the spicules found at earlier periods. S^{35}-uptake of femoral epiphyses in aged animals has not been undertaken; however, Dziewiatkowski (10) did study and compare rats 10, 30, and 300 days of age. The $S^{35}O_4$ activity was highest in 10-day-old rats and lowest in the 300.

In view of a recent investigation by Tonna and Cronkite (19) concerning the uptake of $S^{35}O_4$ by the femoral periosteum of aging rats, it was important to extend such studies to the femoral epiphyses of old animals of at least 104 weeks of age and to make observations prior to, during, and shortly after the period of maximum rate of bone formation. It is hoped that these studies will broaden the understanding of some biochemical changes associated with the skeletal system which occur coincidentally with aging.

MATERIAL AND METHODS

Rats of a Sprague-Dawley strain were divided into 6 age groups, totaling 36 animals. Each group consisted of 6 animals (3 males and 3 females). Group I consisted of 1-week-old rats, Group II of 5-week-old, Group III of 8-week-old, Group IV of 26-week-old, and Group V and VI of 52-week-old and 104-week-old, respectively.

Sterile physiological saline containing sulfuric acid-$S^{35}O_4$ was given in two subcutaneous injections to each animal (400 μc/100 Gm. body weight), 12 hours apart.* Five hours after the last injection the animals were killed by ether. Immediately after death the proximal and distal femoral epiphyses of both legs were removed and placed in a 3:1 mixture of absolute ethyl alcohol and glacial acetic acid for three hours, followed by an additional 24 hours of fixation in formol saline and washing for 24 hours (14). Paraffin sections were prepared without prior decalcification. This was considered essential for preventing alterations by the decalcifying medium. The tissue sections were coated with 1% celloidin solution prior to covering with British Kodak AR-10 stripping film, as was suggested by Messier and Leblond (13) to prevent possible chemographic effects. The autoradiographs were then placed in a cold, dry atmosphere (13). All the emulsions were exposed for 40 days. One set of sections was Feulgen-stained prior to covering with stripping film, and another set was stained with metanil yellow-iron hematoxylin after developing (16). Additional sections were stained routinely with hematoxylin and eosin. The quantitation of results was based on a visual estimation of the autoradiographic density of specific regions under study. Comparisons were always made with the results obtained from sections of Group I animals.

RESULTS

The proximal and distal epiphyses exhibited 5 recognizable zones in the autoradiographs, namely: 1) Zone of resting cartilage, 2) Zone of young proliferating cartilage, 3) Zone of mature cartilage, 4) Zone of calcifying cartilage, and 5) Developing trabeculae of the metaphysis (fig. 1). The localization of $S^{35}O_4$ in these zones was essentially similar at all ages. How-

* Supported by the United States Atomic Energy Commission.

* Obtained from Oak Ridge National Laboratory, Oak Ridge, Tennessee, as carrier-free $H_2S^{35}O_4$ in 0.2 N HCl.

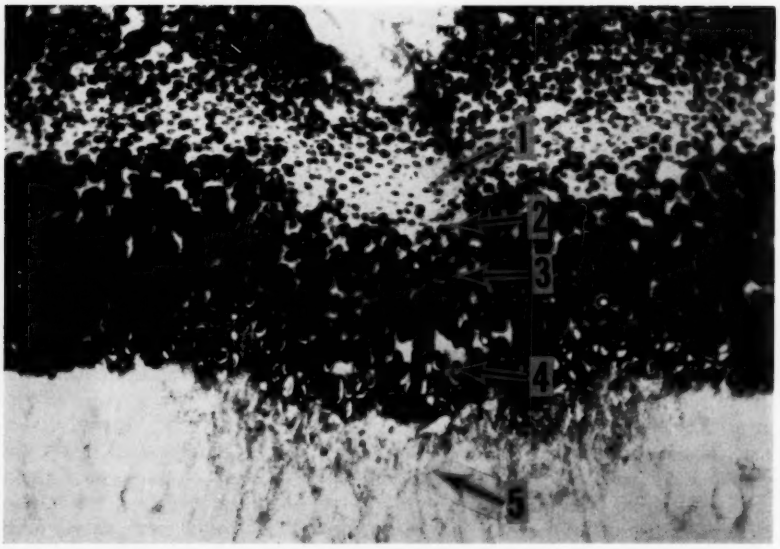
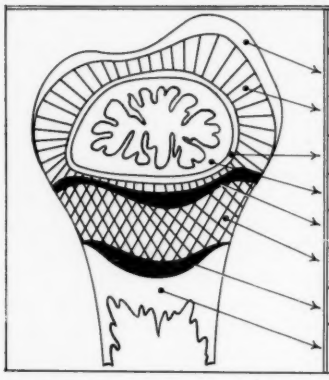


Fig. 1. A $S^{35}O_4$-autoradiograph of the distal femoral epiphysis of a 5-week-old rat. The epiphyseal plate reveals the five recognized zones described in the text (indicated by arrows). X 250.

ever, the level of radioactivity varied from zone to zone and from one age to another (table 1).

The $S^{35}O_4$ uptake was small at the zone of resting cells but large at the zones of young proliferating and hypertrophic mature cells. Since observations were made 17 hours after administration of the isotope, the intralacunar regions revealed the bulk of radioactivity. This is clearly shown in figure 1. Essentially less $S^{35}O_4$ uptake was found in the zones of calcifying cartilage cells and the developing trabeculae of the metaphysis. The $S^{35}O_4$ uptake and distribution of isotope at the secondary centers of ossification were similar to those described for the epiphyseal disk. Autoradiographs showed that the $S^{35}O_4$ uptake became increased from 1 week to 5 weeks of age. The high uptake of radiosulfur by the epiphyseal disk is shown in figure 2A. At this age, bone formation in the rat takes place at a mixiumum rate. The uptake seen at 5 weeks of age was maintained and observed at 8 weeks of age. By 26 weeks the

TABLE I. The $^{35}SO_4$ distribution and activity in the various zones of the distal epiphysis of the femur of rats at different ages.



Age (Weeks)	1	5	8	26	52	104
Zone of resting cartilage	+	++	++	+	±	±
Zone of proliferation and hypertrophy	+++	+++	+++	++	++	+
Zone of calcification	++	++	++	+	±	±
Zone of trabecular formation	+	++	+	±	±	±
Zone of resting cartilage	++	++	++	+	±	±
Zone of proliferation and hypertrophy	++++	+++++	+++++	+++	+++	++
Zone of calcification	+++	++++	+++	+	±	±
Zone of trabecular formation	++	++	++	+	±	±

The activity is indicated by ± to +++++ and represents the extent of grain reduction in autoradiographs.

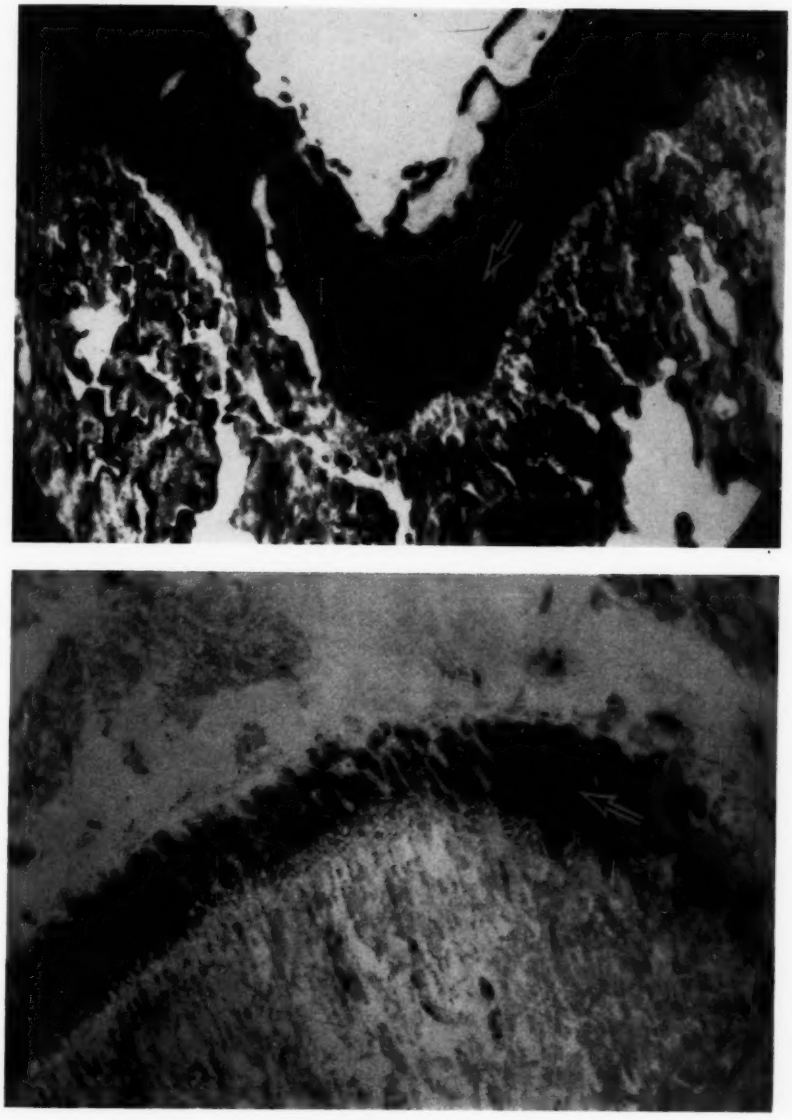


Fig. 2. A comparison between $S^{35}O_4$-autoradiographs of the distal femoral epiphyseal plate of (A) a 5-week-old rat, and (B) a 26-week-old rat. Arrows indicate similar zones. X 150.

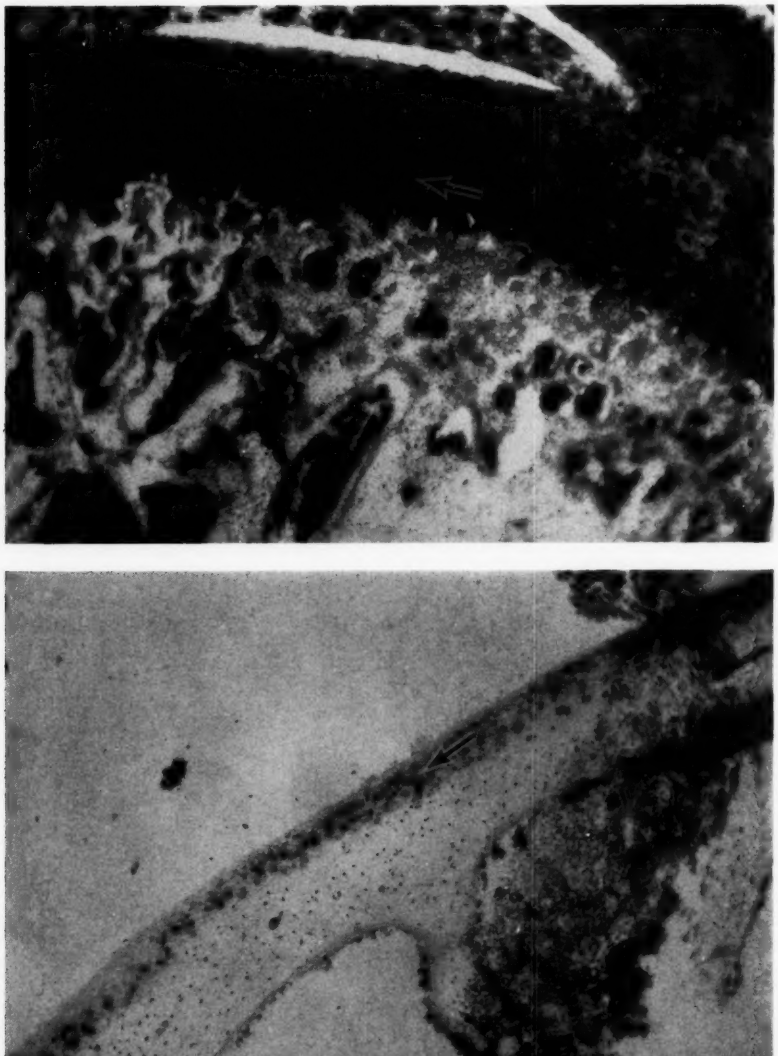


Fig 3. A comparison between $S^{35}O_4$-autoradiographs of the articulating surface of the distal femoral epiphysis of (A) a 1-week-old rat, and (B) a 104-week-old rat. Arrows indicate similar zones. X 250 and X 150.

$S^{35}O_4$ uptake was considerably diminished (fig. 2B). Animals one year of age exhibited a $S^{35}O_4$ uptake which was comparable to the one-half-year-old rats. At 2 years of age, however, the S^{35}-labeling was lower than at any previous age examined. The decreased S^{35} uptake was observed in all epiphyseal zones.

Some familiar histological changes were observed accompanying aging of the epiphysis, which also reflected changes in $S^{35}O_4$ distribution and activity. In the ephiphyseal disk of older animals fewer cells were seen than were usually encountered at about 5 and 8 weeks of age. The cascade of cells making up the proliferative and hypertrophic zones of the epiphyseal disk of old rats did not show the homogenous distribution of radiosulfur seen in younger animals (compare fig. 2A with 2B). $S^{35}O_4$ uptake seemed to be highest at the regions about the periphery of the disk in areas close to the junction of the periosteum and perichondrium (fig. 2B). The proliferative and hypertropic cells at the central aspects of the epiphyseal disk of older animals exhibited the largest $S^{35}O_4$ uptake; however, they revealed a patchy distribution of radioisotope. The uptake varied considerably from one adjacent cell to another.

The cortex of the articulating surface also exhibited an abundant but somewhat lower uptake of $S^{35}O_4$ than the epiphyseal disk. Histologically the cartilage cells were disposed in well-defined zones similar to those which made up the epiphyseal disk. The cascade arrangement of cells of the proliferative and hypertrophic zones of the epiphyseal disk was not seen. Changes in the $S^{35}O_4$ uptake and distribution were the same as those described for the epiphyseal disk (see fig. 3A and 3B). No significant differences were noted between males and females.

DISCUSSION

Radioactive sulfate became predominantly incorporated at the proliferating and hypertrophic zones of the epiphyseal disks and to a lesser degree at comparable zones found below the articulating surface of the epiphyses. This distribution is essentially similar to that found by Dziewiatkowski (10). All the cellular zones recognized in young rats were found in older animals. The width of the zones varied, usually becoming thicker at 5 and 8 weeks of age and thinner with increasing age. This histological change is a consequence of the diminishing proliferative potential of disk cells in older animals observed during present studies employing tritiated thymidine (18).

Logan (12) pointed out that calcification of cartilage was accomplished by a loss of organic sulfate. A reduction in sulfated mucopolysaccharides of cartilage was also shown by Sylvén (17) during mineralization. Siffert (15) and Godard (11) are of the opinion that sulfated mucopolysaccharides of the cartilage matrix are utilized during bone matrix synthesis. The increased $S^{35}O_4$ activity exhibited at the proliferating and hypertrophic zones of the epiphysis, at a time coincidental with the period of maximum rate of femoral growth in the rat, is believed to represent a necessary accumulation of radiosulfate, which will be available for utilization during bone matrix formation. In older animals this utilization was clearly demonstrated. Regions at the periphery of the epiphyseal disk continued to incorporate large amounts of radiosulfur, whereas the central aspects of the disk, where bone growth and matrix production were less, exhibited a much lower $S^{35}O_4$ uptake. This pertinent relationship was recognized by other investigators (1, 6, 7, 10).

Our results also showed that $S^{35}O_4$ and presumably chondroitin sulfate were significantly less in zones of calcifying cartilage than in zones of proliferation and hypertrophy and that this situation persisted throughout the life of the animal. Bélanger (3) showed further that the intracellular accumulation of radiosulfate appeared partially extracellular two days following the administration of tracer in young rats and hamsters and strictly extracellular after 6 days. This finding indicates that the cartilage cells are not only accumulating large quantities of labeled sulfur but also liberating large quantities at the same time, since active bone formation is continually going on in young animals and the formation of bone matrix must be present before ossification takes place. The proliferative and hypertrophic zones of the epiphyses and disk appear to serve as active sites for the formation of large quantities of chondroitin sulfate precursors or, perhaps, production of chrondroitin sulfate necessary for matrix formation.

Apparently in young animals cartilage cells are utilized so rapidly during growth and remodeling that the cells do not remain long enough at the epiphyseal disk and epiphyses to undergo age changes. The rate of cartilage cell

turnover, however, diminishes with increasing age. In older animals fewer epiphyseal cartilage cells are capable of undergoing mitosis. At the same time skeletal growth has slowed down and consequently fewer cells are being utilized in endochondral ossification. The cells making up the epiphyseal disk, therefore, remain in this compartment longer than those of young animals. During this prolonged period cellular age changes take place and are accompanied by a reduction in S^{35} uptake. Previous studies revealed similar findings for periosteal osteoblasts (19).

The precise relation between $S^{35}O_4$ uptake, mucopolysaccharide precursor production, formation of mucopolysaccharide and matrix production is largely unknown. It seems that these parameters are intimately related to one another and are necessary for calcification. S^{35} utilization may be primarily necessary for mucopolysaccharide precursor formation while the final polymer may actually be assembled outside of the cell. Accepting the fact that large polymers of sulfated mucopolysaccarides and collagen form an integral part of the structure of the organic matrix of bone, a reduction in either S^{35}-uptake or collagen formation during aging is expected to result in decreased bone formation.

SUMMARY

An autoradiographic study was made of the variations during aging (36 animals from 1 to 104 weeks of age) in the S^{35}-labeled sulfate uptake of the cellular complement of rat femoral epiphyses. The radioisotope distribution remained essentially the same at all ages; however, the uptake varied with age. Initially there occurred an increase in uptake during the period of 5 and 8 weeks of age, followed by a progressive reduction in the total uptake with increasing age. The changes observed in the radiosulfate uptake of epiphyseal cartilage cells were coincidental with histological and cytological changes representative of reduced endochondral bone formation and epiphyseal aging.

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CALCIUM, CHOLESTEROL, AND COLLAGEN LEVELS IN HUMAN AORTAS

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Numerous reports have appeared in the literature regarding the composition of human aorta in health and disease. These studies at first concerned a single aortic component such as calcium (2, 4) or cholesterol (26). With time, similar and additional studies began to emerge and cover greater numbers of aortic constituents which were explored to a greater degree (7-10, 14, 16-22, 27). In recent times the emphasis has been on serum changes as affected by arterial disease (1, 6). Although this wealth of information sheds considerable light on the complexity of the chemistry of the arterial wall, a great deal more remains to be accomplished before the processes of changes in the aorta accompanying age and disease can be clearly understood.

This study has as its purpose the examination of a large number of human aortas for calcium, cholesterol, and collagen in those sections of aorta which are not affected by atheroma or fatty streaking and to relate these findings to age and sex. The incentive is derived from a previous study (14) wherein it was demonstrated that the aorta has an inherent ability to bind calcium. This, together with the close association between calcium and cholesterol in plaques and calcium and collagen in mineralization, suggested the investigation.

MATERIAL

Aortas from 40 female and 82 male subjects were examined. These individuals ranged in age from fetus to 80 years. The freshly collected vessels were stripped of their adventitia tunica and washed under cold, running, tap water. These were then cut longitudinally, placed between filter paper, and weighted down with lead bricks. No attempt was made to separate the intima from the media layer. The aorta strips were removed after 72 hours and examined macroscopically for the purpose of selecting only the completely plaque-free areas and only those areas considered completely free of fatty streaking. The selected sections were then cut into small pieces, approximately 1 × 2 mm., put into 5 dram vials, and placed in a desiccator for further drying. Usually one full week was sufficient to obtain constant weights and render the samples suitable for analysis.

The selected aortas were from subjects with cause of death distribution as follows:

	Number of Subjects		
Cause of Death	*Female*	*Male*	*Total*
Carcinoma	11	23	34
Coronary heart disease	9	21	30
Congenital heart disease	8	8	16
Cirrhosis of the liver	2	6	8
Miscellaneous diseases*	7	20	27
Accident, fire, poison	3	4	7
Totals	40	82	122

METHODS

The analyses for calcium, cholesterol, and hydroxyproline were made on the same aliquot sample of the dried material. The determinations were carried out in duplicate with less than 3% variation between replicate analyses of the same material. This aliquot sample ranged in weight from 40 to 80 mg. The extraction of fat was carried out with ethyl ether in a Soxhlet apparatus over a period of 28 hours. We have found that cholesterol was quantitatively removed in this period of extraction.

The fat-free residue was then hydrolyzed with 6N HCl in a manner previously described (13), and the hydrolyzate analyzed for calcium and hydroxyproline.

Cholesterol.—The ether extracts were transferred quantitatively into 125 ml. Erlenmeyer flasks and allowed to dry under forced air. The dried residue was next extracted with chloroform and analyzed for total cholesterol using the method of Bloor (3).

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* Kidney disease, multiple myeloma, Hodgkin's disease, and lupus erythematosus disseminatus.

Hydroxyproline. — Two ml. aliquots of the clear, filtered hydrolyzate were transferred to a 25 ml. volumetric flask, neutralized with ammonium hydroxide, and diluted to volume. The hydroxyproline determinations were then carried out according to the method of Neuman and Logan (23). Conversion to collagen was made by the use of a 7.46 factor.

Calcium.—Fifteen ml. of the above hydrolyzate were placed into a 45 ml. Vycor dish and evaporated to dryness, under hood, by means of gentle heating. The dishes were then placed in the muffle furnace. The temperature was raised slowly to 550 C. and allowed to remain for 24 hours. After 24 hours, the furnace was turned off and the samples allowed to cool slowly. The cooled samples were treated with hot, concentrated hydrochloric acid and then hot, diluted acid. The washings from each sample were pooled, neutralized with ammonium hydroxide, and analyzed for calcium according to the method of Wang (25).

RESULTS

The results of calcium, cholesterol, and collagen analysis are presented in tables 1 and 2 and are illustrated graphically in figures 1-3. The data are represented so that points falling between two decades are averaged as the higher decade.

Beginning with the collagen data (table 1), it is evident that collagen content of the aorta varies but little during one's life span. A slight, progressive decrease is actually encountered, leveling off at the fourth decade. This is true for both sexes, whose values are interchangeable.

An examination of the calcium data, on the other hand, reveals a constant increase beginning at the second decade. The rate of increase seems greater for the male than the female. It is only between the sixth and seventh decade

TABLE 1. COMPOSITION OF ATHEROMA-FREE HUMAN AORTAS IN MALES AND FEMALES.

Age Groups (Years)	Subjects Studied	Grams per Kilogram of Dry Vessel		
		Calcium	Cholesterol	Collagen
Fetus	3	1.0	6.3	312.6
0- 9	28	0.7±0.4*	3.8± 0.9*	255.8±56.3*
10-19	8	0.7±0.3	5.3± 1.6	205.1±17.7
20-29	6	1.8±1.0	9.9± 6.6	199.0±21.5
30-39	10	3.2±1.3	11.3± 3.6	185.0±36.1
40-49	16	4.8±1.6	22.8± 9.5	203.1±28.6
50-59	16	4.6±2.3	17.6± 2.2	219.6±42.5
60-69	20	8.4±3.6	55.9±25.8	217.0±50.4
70-79	15	7.1±5.6	46.2±31.5	217.5±46.0

* Standard Deviation.

TABLE 2. COMPOSITION OF HUMAN INFERIOR VENA CAVA IN MALES AND FEMALES.

Age Groups (Years)	Subjects Studied	Grams per Kilogram of Dry Vessel		
		Calcium	Cholesterol	Collagen
0-79	14	0.4±0.2*	7.0±3.4*	368.7±59.6*

* Standard Deviation.

Fig. 1. Figure 1 represents the log of average aorta concentrations of calcium, cholesterol, and collagen versus the age of males and females. The mean values were calculated on the basis of dry tissue weight.

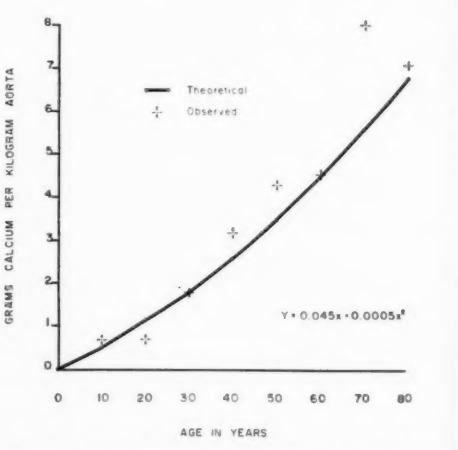

Fig. 2. The calcium content of the aorta of different ages.

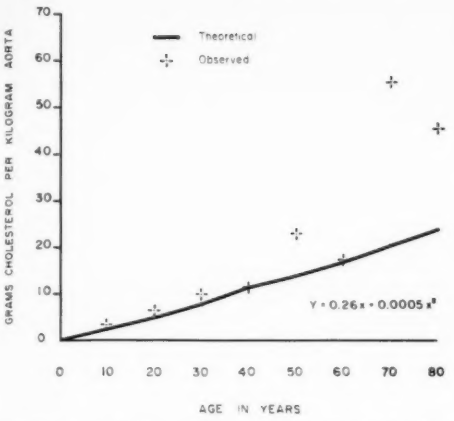

Fig. 3. The cholesterol content of the aorta of different ages.

that the female calcium levels catch up with and exceed the male values.

The situation is almost identical in the case of cholesterol. The rate of accretion is more rapid in the male than the female, and only between the sixth and seventh decades do the female values equal and exceed those of the male. The parallelism existing between the calcium and cholesterol data is marked.

Examination of the vena cava in the same manner as the aorta reveals no differences in the respective components that could be ascribed to either age or sex. The data are shown in table 2. The most striking difference appears in the chemical composition of the vena cava and the aorta. The average collagen concentration of the vena cava is approximately 78% greater than the average adult collagen concentration of the aorta. Furthermore, no accumulation of calcium or cholesterol takes place in the vena cava in contrast to the aorta.

DISCUSSION

The data presented herein find ample verification in previous reports in the literature. The increase of calcium in the aorta with age has been reported by Baldauf (2), Blumenthal and associates (4, 5), Lansing and associates (19, 20), Faber and Land (12), Kvorning (18), Buck (7, 8), and Zinsser (27). Essentially, the present results depicted in table 1 are in agreement with those previously reported.

In a similar manner, cholesterol concentrations have been reported by Windaus (26), Schonheimer (24), Meeker and Jobling (21), Buck (7), and Faber and Lund (12). The increase of cholesterol content with age obtained in the present report duplicates the results of the earlier studies.

Reports of the collagen content of the aorta seem to be less numerous than those of calcium and cholesterol. Myers and Lang (22) examined 83 aortas from subjects ranging in age from 15 through 88. The mean collagen content was constant, 15.5% in a dry weight basis in ages up to 44 years. From that time through 88 years the collagen level rose up to 19.1%. Buddecke (9, 10) reported an average of about 22% on a dry weight basis with a range of 17-28%. The present study is in agreement with these results. The discrepancy with the earlier study may very well be explained by the non-specific methods used for collagen determination prior to 1950.

In the present study, determinations of the three constituents were performed on the same specimen, which itself was carefully chosen to be plaque-free. This is an important consideration when interrelationships are sought, and it is especially true for the aorta where we have found a considerable variability in the concentration of a constituent in different specimens from the same vessel. This undoubtedly is due to the heterogeneous dispersal of these constituents in the vessel.

When the calcium and cholesterol averages for males are plotted (figures 2 and 3) directly instead of a logarithmic function, two parabolic curves are obtained, indicating their interrelationship. The empirical equation for the calcium accretion is $y = 0.045x + 0.0005x^2$, where y is the calcium content in grams per kilogram of aorta and x is age in years. The index of correlation of the experimental points to the theoretical computed according to Ezekiel (11) is 0.86, which is a satisfactory agreement.

The empirical equation for cholesterol accumulation is $y = 0.26x + 0.0005x^2$, where y is the cholesterol content in grams per kilogram of aorta and x is again the age in years. The index of correlation of the experimental points is 0.54, which may be considered fair. However, in the light of the diversity of diet and disease in the cases, the correlation must be considered satisfactory.

The accumulation of calcium by the aorta and the absence of accretion in the vena cava is consistent with the previous evidence demonstrating that the aorta has an inherent ability

to bind calcium (14), whereas this characteristic is absent in the vena cava (15). The many components in the aortic wall which have been shown capable of binding calcium (15) are responsible for the complexity of the process which is reflected in the parabolic form of the equation. In the case of cholesterol, it has been shown previously (14) that calcium bound by the aorta has a marked ability to disrupt emulsions containing cholesterol. This establishes the relationship between calcium and cholesterol in plaque formation, a relationship which is present in the pre-plaque stage as reflected in the similarity of the curves in figure 1.

No apparent correlation exists between collagen and calcium or cholesterol deposition as depicted in figure 1. This is consistent with the *in vitro* finding that the calcium binding factors of the aorta may be completely removed leaving the collagen intact (15).

SUMMARY

A total of 122 human aortas from both sexes were examined for calcium, cholesterol, and collagen. Chemical analysis of atheroma-free sections revealed that the collagen level, although somewhat higher in the children group, remains relatively constant, about 20%, with increase in age, irrespective of sex or disease.

Calcium concentrations rise gradually from 0.07% in children to 0.84% in the 60-69 year group, following the empirical equation $y = 0.045x + 0.0005x^2$ for the males. Concentrations for the female aorta are considerably lower up to about 65 years of age. From then on the calcium levels in the female aorta rise sharply.

Cholesterol levels increase constantly from 0.38% in the children's group to 5.5% in the 60-69 year group, following the empirical equation $y = 0.26x + 0.0005x^2$ for the male. Female levels are somewhat lower than those of males up to about 65 years. Above that age, female cholesterol levels rise sharply.

Vena cava from both male and female subjects reveal low calcium and cholesterol values and high collagen concentrations. Average levels are 0.04%, 0.7% and 36.8% respectively.

The present data are discussed in relation to previous findings concerning aortic plaque formation and are found consistent with them.

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SKIN REFLEX AND VOLUNTARY REACTION TIMES IN YOUNG AND OLD MALES

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The time required by humans to respond voluntarily to various types of external stimuli has been shown to increase with increasing age (1, 2, 6, 8). Lele and associates (4) showed that touch reaction times were more prolonged in the case of less intense stroking stimuli than in the case of more intense punctuate stimuli to the skin of the finger. Magladery and associates (5) did not find a significant increase in reaction time to touch in their 14 subjects between 61 and 85 years of age when they were compared with 9 subjects between 22 and 46 years of age. They did report, however, a significant increase in plantar flexor reflex latency and superficial abdominal reflex latency in their older subjects. Pedersen (9) has reviewed the evidence regarding two possible mechanisms of reflexes (one which assumes a spinal pathway and the other which assumes a more central pathway) and concludes that the assumption of spinal pathways for reflexes is probably correct. The present paper was designed to determine the effects of age on (a) reaction time to touch and (b) on plantar and abdominal reflex trends.

METHODS

The children tested ranged from 3 to 14 years of age and were selected from the population of the Pediatric Outpatient Clinic of the Baltimore City Hospitals. The adults, who ranged from 20 to 98 years of age, were patients, employees, and staff members of the Baltimore City Hospitals Infirmary Division (Old People's Home). Subjects were free of disturbances of the central and peripheral nervous system as judged by physical examination and history.

Tests were performed with the subject in the dorsal recumbent position. For the foot reaction time and reflexes, the muscle action potentials were led from small solder electrodes placed over the small muscles of the left foot through paired leads and a preamplifier to a dual beam cathode ray oscilloscope. The subjects were connected with ground through a saline moist pad placed around the leg just above the ankle. The action potentials were recorded photographically from the oscilloscope screen.

Tactile stimuli for eliciting reflexes and voluntary muscle reactions were provided by a plastic rod tapered to a dull point at one end. Contacts were arranged in the handle of the rod so that at the instant of contact with the skin the beam of the cathode ray oscilloscope was triggered. The reflex and reaction times were measured by determining the time interval between the beginning of the cathode ray beam and the beginning of the muscle action potential. A time calibration curve (10 msec.) was recorded on the second synchronized beam from the output of a standard oscillator.

Plantar flexor reflexes were elicited by a brief longitudinal scratch to the sole of the foot in the area in which the shortest, most consistent responses were elicited. The length of this scratch was approximately 5 cm., and the duration approximately 200 msec. The intensity of scratch necessary to elicit flexion potentials ranged from a mere touch to a firm stroke. In no case was the stimulus judged painful by the subjects. Foot reaction times were stimulated by touching the sole of the foot. The subject was instructed to plantar-flex his foot as soon as possible after the touch.

The abdominal reflexes were elicited by a brief gentle downward scratch to the skin along the rectus muscle slightly to the left of the midline and above the navel. This reflex was recorded from a pair of electrodes, which were affixed to the skin just under the left front margin of the ribs in the mid-clavicular line at the site of the circumscribed reflex movement. The ground pad was placed across the middle of the chest.

Fifty or more stimuli of each type were administered to each subject at each sitting. Average values for both reflex and reaction time were calculated if 9 single values were obtained

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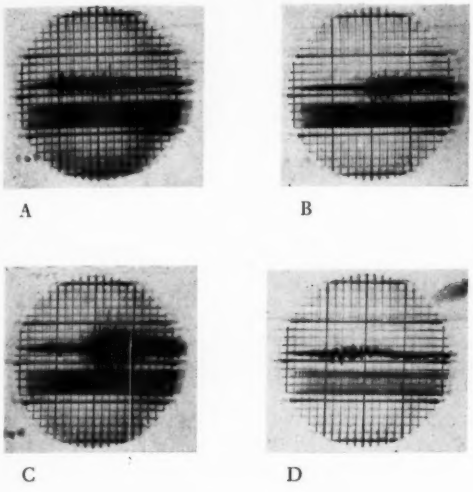

Fig. 1. Action potentials of small muscles of the foot and of abdominal muscles of an 81-year-old man. Time interval of 10 msec.

(A) Plantar flexor reflex response obtained with brief scratch (105 msec.).

(B) Voluntary flexion of left foot (right foot stimulated) (215 msec.).

(C) Voluntary flexion of left foot (left foot stimulated), (225 msec.). Voluntary reaction preceded by reflex response (105 msec.) to touch in subject with high reflex sensitivity.

(D) Abdominal reflex response (80 msec.).

TABLE 1. NUMBER OF SUBJECTS IN WHOM TESTS WERE ATTEMPTED COMPARED WITH NUMBER OF SUCCESSFUL RESULTS FOR REACTION TIME AND REFLEX TIMES.

Age (Years)	Reflex Times				Reaction Time	
	Foot		Abdomen		Foot	
	T*	S†	T	S	T	S
3- 9	35	12	29	15	11	8
10-19	7	6	8	5	10	7
20-29	13	10	8	2	19	19
30-39	14	8	10	6	23	23
40-49	6	5	3	1	8	8
50-59	11	8	5	5	13	13
60-69	12	10	6	5	15	14
70-79	15	12	5	5	15	14
80-89	9	8	3	3	7	4
90-98	2	2	0	0	2	2
Total	124	81	77	47	123	112
Percentage Successful		65%		61%		91%

* Tests attempted.
† Tests successful.

TABLE 2. DAY-TO-DAY VARIABILITY OF PLANTAR REFLEX LATENCIES ELICITED BY BRIEF SCRATCH IN NINE SUBJECTS.

		Reflex Latencies (msec.)		
Age	Day	Average	Difference	% Difference
60	1	85		
	2	96	11	12
67	1	84		
	2	93	9	10
69	1	92		
	2	86	6	7
73	1	99		
	2	96	3	3
74	1	81		
	2	80	1	1
78	1	95		
	2	88	7	8
81	1	97		
	2	90	2	2
82	1	94		
	2	93	1	1
86	1	70		
	2	93	23	28
Range			1-23	1-28

from the records taken. For each subject mean values for reaction time were calculated after the extreme high and low values which were separated from the remainder of the distribution by an interval of more than 15 msec. were excluded.

Statistical calculations were performed according to methods described in Snedecor (11).

RESULTS

Sample recordings of action potentials of small muscles of the foot are shown in figure 1 to illustrate the types of responses obtained in the same subject. Among the subjects tested, reaction times for the foot were successfully elicited in 91% of the cases, in contrast to reflex responses which were obtained in only 65% of the subjects (table 1). Abdominal reflex times were elicited in 61% of the cases. Although there is some indication that failure to elicit voluntary reaction times occurred more frequently among the children and older subjects than among the middle-aged, there was no systematic age difference in failure to obtain reflex time measurements. There was no difference in our ability to elicit the various reflexes.

Table 2 gives a comparison of the day-to-day variability of reflex times for 9 individuals tested on two different days. Differences were expressed as percentage of the best estimate of each measure for each individual (mean of two days) and ranged from 1 to 28%.

Table 3 shows the range of average values and the means with their standard deviations

TABLE 3. MEAN VALUES OF REFLEX AND REACTION TIMES BY AGE DECADES.

Age (Years)	Reflex Times (Brief Scratch)						Voluntary Reaction Time		
	Foot			Abdomen			Left Foot		
	N	Mn.± σmn. (msec.)	Range (msec.)	N	Mn.± σmn. (msec.)	Range (msec.)	N	Mn.± σmn. (msec.)	Range (msec.)
3- 9	12	85±4.57	56–110	14	60±2.22	45–73	8	247±11.43	205–299
10–19	6	88±5.80	70–111	5	60±4.62	46–70	7	210±10.23	176–262
20–29	10	90±2.50	78–102	2	70	63–76	19	178±3.76	143–207
30–39	8	101±5.66	70–119	6	71±5.36	55–87	23	177±3.76	134–214
40–49	5	99±8.34	81–121	1	40	40	8	184±7.95	148–222
50–59	8	101±6.01	78–130	5	65±4.61	57–83	13	192±5.28	167–227
60–69	10	99±3.47	84–119	5	59±6.29	37–74	14	214±6.43	179–233
70–79	12	97±4.48	66–119	5	74±9.24	42–96	14	222±8.73	177–293
80–98	10	95±7.06	70–143	3	82	63–95	5	229±12.75	189–269
0–98	81	94±1.78	56–143	46	65±2.04	37–96	111	199±3.04	134–299

for each age decade for reflex and reaction times.

Foot reaction time and plantar reflex time are plotted for individuals against age in figure 2. In the age group 20 through 98, average voluntary foot reaction time increased significantly with age ($P < .001$) at the rate of 1 msec. per year*.

The children were found to have significantly longer reaction times than the young adults ($P < .001$ for the age group 0-9 years vs. young adults and $P < .005$ for the age group 10-19 years vs. young adults).

On the other hand, the reflex times showed no change with increasing age. At any age the longest brief scratch reflex time was shorter than the fastest reaction time (fig. 2).

No significant age differences were found in times for the superficial abdominal reflexes which averaged 65 msec. (fig. 3).

* The regression equation of voluntary reaction time on age was: reaction time (msec.) = 0.96 age (years) + 147.

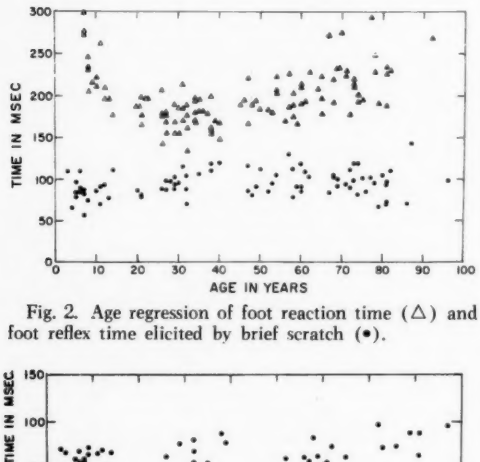

Fig. 2. Age regression of foot reaction time (△) and foot reflex time elicited by brief scratch (•).

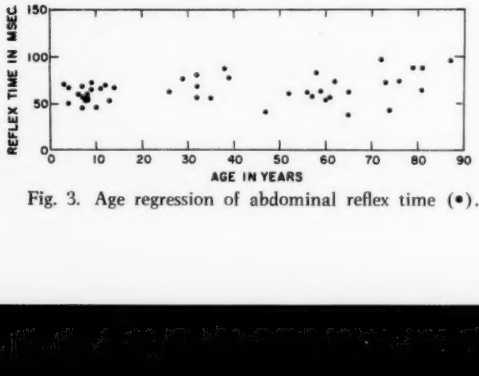

Fig. 3. Age regression of abdominal reflex time (•).

DISCUSSION

In contrast to previous studies, which indicate a lengthening of plantar reflex times with age following the conventional scratch stimulus (5), no significant age increment in reflex time following the administration of a brief scratch to the sole of the foot was observed in the present study. The evidence concerning the effects of intensity of the stimulus on reflex time is conflicting. Eccles and Sherrington (3) as well as Riddoch (10) and Pedersen (9) have reported that with mild stimulation reflex times are longer than with strong stimuli. On the other hand Magladery and associates (5) found no alteration in reflex times with changes in intensity of the stimulus. Although no measurements of stimulus intensity were made in the present study, it is our impression that increasing the intensity of the short scratch stimulus did not result in a systematic shortening of the reflex times. If thresholds of stimulation of reflexes or the relationship between threshold and reflex latency changed with age, there was no systematic effect on reflex latency or its variability among subjects in the various age decades tested.

Data from the present study show a significant increase in voluntary reaction time to touch when applied to the sole of the foot in mature subjects. These findings are in agreement with previous studies reporting increased reaction time to stimuli from other sense modalities (1, 2, 6, 8). Thus age differences become most apparent in latencies of voluntary responses involving the participation of higher levels of the central nervous system. Although Wayner and Emmers (12) have reported an increase in spinal synaptic delay in old compared with young rats, it is questionable whether age differences in reaction time can be ascribed to structural changes in the nervous system alone.

Although there is a slight slowing in the speed of conduction of the nerve impulses in peripheral nerves with advancing age (7) it can make only a minor contribution to the lengthening of reaction times with age. Another study (2) has shown that the length of the neural pathway is of minor importance in explaining age differences in reaction time.

It therefore seems probable that the increased latencies for reaction time observed in the present study must be associated with functional changes in the central nervous system.

SUMMARY

In 81 subjects aged 3-98 years, plantar reflex latencies to a brief scratch averaged 94 $\pm$ 1.8 msec. for subjects of all ages. The corresponding mean value for the abdominal reflex observed in 46 individuals was 65 $\pm$ 2.0 msec. No significant change with age was observed for either type of reflex.

Voluntary reaction time to touch of the left foot was measured in 111 subjects aged 7-92 years. The reaction times were found to be significantly increased in young children and in elderly subjects as compared with young and middle-aged adults ($P < 0.001$). Mean values were: age 10-19 yrs., 210 $\pm$ 10.2 msec.; age 30-39 yrs., 177 $\pm$ 3.8 msec.; age 70-79 yrs., 222 $\pm$ 8.7 msec.

It is concluded that the slowing of voluntary reaction time to touch with increasing age is due primarily to functional alterations in the central nervous system.

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SERUM LEVELS OF ANTIBIOTICS IN YOUNG AND OLD SUBJECTS FOLLOWING ADMINISTRATION OF DIHYDROSTREPTOMYCIN AND TETRACYCLINE

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In previous investigations by the present authors (1, 3) the concentrations of G-penicillin and procaine penicillin in serum and in cantharidin-induced blister fluid were determined in young and old subjects and were found to remain at significantly higher levels in the old than in the young individuals. The present study was undertaken with the purpose of investigating whether the administration of two other antibiotics, dihydrostreptomycin and tetracycline, to young and old subjects similarly would be followed by the occurrence of different serum levels.

MATERIALS AND METHODS

Twenty-six young persons (9 males and 17 females, age range 18-33, mean age 26.8 years; weight range 41.5 to 85.9 Kg., mean weight 63.3 Kg.) and 27 old subjects (12 males and 15 females, age range 63 to 87 years, mean age 75.4 years; weight range 42.2 to 85.8 Kg., mean weight 62.4 Kg.) were included in the study. All the individuals were hospitalized patients who, according to their medical history, physical examination, and urine tests, did not present signs of renal insufficiency. Determinations of the plasma NPN concentration were made in 25% of the elderly patients; the observed values ranged between 29 and 39 mg.%. Examination of catheterized urine specimens in general showed normal findings except in the case of one old patient, who exhibited slight proteinuria.

In the investigations with dihydrostreptomycin,* 1.0 Gm. of this compound was administered intragluteally, and blood samples were drawn 1, 12, 24, and 36 hours after the injection. The dihydrostreptomycin dose of 1.0 Gm. was used irrespective of the subjects' body weight. The serum concentration of the antibiotic was determined by the modified (6) WHO Cup-Plate method, using *Bacillus subtilis* as the test microorganism.† The studies on tetracycline‡ were performed by intragluteal injection of 100 mg. of the compound and by collection of blood samples 1, 6, and 12 hours following the injection. The tetracycline serum concentrations were likewise determined by the modified (6) WHO Cup-Plate method, using *Bacillus cereus* as test microorganism.† Neither the administration of dihydrostreptomycin nor tetracycline was accompanied by any side effects.

RESULTS

The observations on the serum antibiotic levels are presented in tables 1 and 2. As seen from the tables, the serum concentrations of both dihydrostreptomycin and tetracycline were found to be higher in the old than in the young individuals. The statistical significance of the differences in concentration was tested by Student's t test. The ½-hour values showed no significant difference between the young and the old individuals for either of the antibiotics. The 12-hour and 24-hour differences for dihydrostreptomycin were highly significant ($P < 0.010$ and $P. < 0.005$); the significance of the 36-hour difference cannot be determined, since the values yielded by the disc method with very small titers are not sufficiently accurate. For tetracycline, the 6-hour difference is probably significant ($P < 0.100$) and the 12-hour difference highly significant ($P < 0.005$).

DISCUSSION

Antibiotics administered intramuscularly are excreted nearly exclusively through the kidneys. Approximately 80% of the penicillin is known to be removed by tubular secretion (3), whereas both dihydrostreptomycin (2, 4) and tetracycline (7, 8) are removed chiefly through the glomeruli. Irrespective of the secretion mech-

* Hydromycin inject., Medical Suppliers Orion, Helsinki.

† The determinations were made by Mrs. Merimaija Kyti, M.Sc., of the Microbological Laboratory of Medical Suppliers, Orion, Helsinki.

‡ The tetracycline (Achromycin®) for this study was supplied through the courtesy of Lederle Laboratories Division, American Cyanamid Company, Pearl River, New York.

TABLE 1. DIHYDROSTREPTOMYCIN, SERUM LEVELS.

No.	1 Hour	12 Hours	24 Hours	36 Hours
Old Patients				
1	4.25	2.30	1.20	0.90
2	13.50	9.80	3.20	1.90
5	10.50	9.80	2.90	0.90
6	18.80	2.30	1.10	0.10
7	11.50	3.80	1.90	1.00
8	10.80	2.50	0.80	0.55
12	9.90	4.20	1.50	0.30
13	7.50	3.50	0.80	0.25
14	7.20	2.10	1.50	<0.10
18	5.50	3.10	0.50	<0.10
19	11.50	3.00	2.80	<0.10
20	17.00	4.00	0.75	0.70
23	10.00	4.20	0.95	0.93
24	9.60	0.80	0.70	<0.10
25	15.00	5.80	1.00	0.88
26	15.00	11.50	2.50	....
	10.7±1.6	4.4±1.1	1.4±0.2	0.56
Young Patients				
3	10.60	0.75	0.10	<0.10
4	9.60	5.60	1.40	<0.10
5	15.00	3.20	0.25	<0.10
6	20.00	1.20	0.70	0.60
7	9.20	1.90	0.90	<0.10
8	10.90	2.00	0.50	<0.10
9	9.80	1.70	1.40	<0.10
10	10.50	3.00	1.50	0.25
12	11.50	1.20	0.10	<0.10
15	19.50	1.50	0.10	<0.10
16	11.00	0.75	0.10	<0.10
21	10.30	0.90	0.10	....
22	4.50	1.20	0.10	....
23	15.00	2.60	0.50	<0.10
24	8.50	1.20	0.10	<0.10
	11.7±1.0	1.9±0.3	0.5±0.1	<0.15

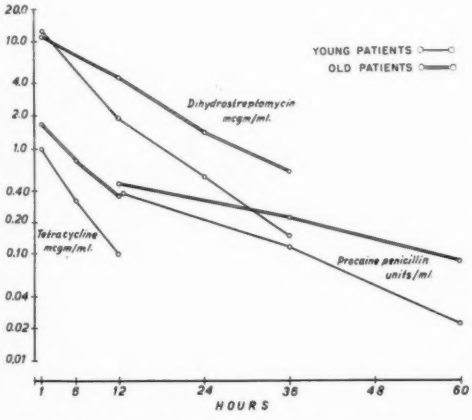

Fig. 1. Serum levels after intramuscular injection of three antibiotics in young and old subjects. A logarithmic scale is used on the ordinate to designate the serum levels. The procain penicillin data are copied from a previous publication (9).

TABLE 2. TETRACYCLINE, SERUM LEVELS.

No.	1 Hour	6 Hours	12 Hours
Old Patients			
3	0.75	0.42	0.30
4	0.16	0.16	<0.10
9	3.50	2.40	0.36
10	1.71	0.54	0.36
11	1.60	1.60	0.30
15	0.39	0.15	0.15
16	4.80	0.60	0.60
17	0.90	0.66	0.60
21	1.29	0.51	0.42
27	0.75	0.35	<0.10
	1.57±0.44	0.74±0.23	0.32±0.05
Young Patients			
1	0.51	0.10	<0.10
2	0.96	0.10	<0.10
11	1.52	0.15	<0.10
13	0.60	0.42	<0.10
14	0.75	0.45	<0.10
17	0.90	0.36	<0.10
18	1.50	0.60	<0.10
19	0.90	0.10	<0.10
20	1.20	0.48	<0.10
25	0.75	0.10	<0.10
26	0.96	0.33	<0.10
	0.96±0.09	0.29±0.05	<0.10

anism, the differences in mean titers of old and young patients with various antibiotics seem to be of the same degree of magnitude (fig. 1). The results are in accordance with the observations of Davies and Shock (5), Miller, McDonald, and Shock (10), and Shock (11), which indicate that both the glomerular function and tubular secretory capacity are reduced with advancing age. It is seen from the diagram that the geriatric group reaches the same low concentration toward the end of the curve much later than does the group of the young patients; with procaine penicillin the difference in time is approximately 18 hours, with dihydrostreptomycin 13 hours, and with tetracycline 6 hours. In order to maintain an identical active concentration in the serum, the intervals between medicinal injections in old patients should be adjusted in accordance with these delays.

SUMMARY

Determinations were made in separate experiments of the serum levels of dihydrostreptomycin and tetracycline following intramuscular injections of, respectively, 1 Gm. and 100 mg. of these antibiotics to 26 young and 27 old individuals. The investigation revealed significantly higher serum concentrations of dihydrostreptomycin in the old than in the young sub-

jects 12 and 24 hours following the administration of this compound. For tetracycline, the 12-hour difference between the serum levels observed in the two groups of subjects was also highly significant.

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A REVIEW OF PROCAINE-THERAPY IN ELDERLY INDIVIDUALS

PAUL LÜTH, M.D.*

Aslan, Director of the C. F. Parhon Institute of Geriatrics in Bucharest, made the observation that patients suffering from painful joint diseases who received injections of procaine not only were relieved of their pains as the result of the local anesthesia but also after a longer period of procaine therapy frequently felt healthier and more active. This side effect was developed by Aslan into a special procaine therapy for old individuals. She named the procaine Compound H_3 in order to indicate that the rejuvenative action was not identical to the ordinary procaine effect.

In 1956 (1) and 1957 (2) Aslan reported her observations on the procaine therapy in a total of 15,000 patients at the West German Congress on Therapeutics. Some of the subsequent studies on Aslan's therapy have been partly confirmatory (4, 6, 7, 8, 13, 14), whereas others have been more critical (5, 10, 12) of the results of the procaine treatment. Since the present author has now completed the treatment of 500 patients according to Aslan's method over a 3-year period, it would seem reasonable to submit a report of these observations.

The Aslan procedure consists of slow intramuscular injection of 5 ml. of a 2% solution of procaine, corresponding to a dose of 100 mg. Twelve successive injections constitute one series of treatment, which is followed by a 2-week pause, after which another series of 12 injections is administered. The procaine treatment is continued for one year or longer. According to personal information received from Aslan, one cannot expect any therapeutic effect until 4 series of treatment have been given.

The procaine solution employed by Aslan has a pH of 4.5. The pH of the solution would not seem to be of great importance, since the rate of decomposition of procaine is rather independent of the pH. One might get the impression that Aslan's constant emphasis on this point was made with the purpose of creating the impression that the procaine drug she uses is a special compound. That is, however, not the case, since Aslan uses ordinary epinephrine-free procaine. I have used Novocain zur Therapie (Hoechst) and have further employed various combinations of procaine with vitamins and with a solution of bee honey (10). A list of the preparations is contained in table 1, which shows that the various preparations are essentially similar with regard to their effect. The manufacture of several different procaine preparations in West Germany is due to the fact that the West German pharmaceutical firms gratefully accepted the opportunity provided by Aslan for the sale of procaine compounds. Aslan subsequently in 1959 issued the statement through the Roumanian commercial delegation that she has not given authority to any firm to use her name. This is, of course, only a rhetorical issue, since procaine is a nonpatented compound. It should be pointed out that Parhon himself already has investigated the effectiveness of a combination of procaine and vitamin E and that this investigation obviously was done with the purpose of studying whether such combination would potentiate the procaine effect.

The most significant obstacle to the procaine therapy is the fact that the patients in Western countries rarely agree to three injections of procaine in a week for a long time when the treatment does not show any immediate effect. Even inmates of institutions for old people object to the prolonged therapy when no improvement is apparent. In the Geriatric Institute in Bucharest the situation may of course be simpler.

With regard to table 1, it should be pointed out that the headings "Improvement" and "No Improvement" represent a simplified classification of the observed therapeutic results. Thus, aggravation of the disease is included in the "No Improvement" group. The treatment in all instances consisted of at least 48 injections, corresponding to 4 series of injections as proposed by Aslan.

In contrast to Aslan's therapeutic procedure, the interval between two series was never extended to more than one week. This seems to be important because the effect of the therapy apparently is dependent on the accumulation of procaine or its decomposition products. In another study (12), Aslan's treatment schedule has been modified in such a way that 30 con-

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TABLE 1. EFFECT OF TREATMENT WITH VARIOUS PROCAINE PREPARATIONS.

Drug Used	Composition of Drug	Number of Patients	Improvement	No Improvement
Gerioptil pro injectione (Fischer)	Procaine + Vitamins B^1, B^2, B^6, Nicotinamide, Sodium pantothenate, inosite, PAB, Vitamin C	163	95	68
Prokopin "G" (Woelm)	Procaine-Procaine glucoside, bee honey solution M^2 "Woelm", Rutin, Sodium glutamate	189	102	87
Hormo-Gerobion (Merck)	Procaine + sex hormone, Triodothyronin, Vitamins A, B^1, B^2, B^6, C, D, P, Inosite, Choline bitartrate	44	35	9
Novocain zur Therapie (Hoechst)	2% solution	74	48	26
Total		470	280	190

secutive injections are given at a rate of three injections weekly.

I have not been able to confirm Schölzel's statement (14) that a change from intramuscular to intravenous administration of the procaine accelerates or potentiates the effect of the drug.

TABLE 2. RESULTS OBTAINED THROUGH TREATMENT OF VARIOUS DISEASE CONDITIONS WITH ASLAN'S PROCAINE THERAPY.

Disease Condition	Number of Cases	Objectively Demonstrable Improvement	Subjective Improvement	No Effect	Aggravation of Condition
Senile mental depression	12	5	4	7	..
Primary and secondary chronic arthrosis	53	8	..	45	..
Rheumatoid arthritis	64	4	..	60	..
Arteriosclerosis, general complaints	153	96	29	28	..
Bronchial asthma	13	2	..	8	3
Cerebral arteriosclerosis, with initial mental deterioration	14	3	..	11	..
Diabetes mellitus					
a. dietary therapy only	15	9	..	6	..
b. peroral antidiabetic drugs	12	9	..	3	..
c. insulin	3	..	..	1	2
Hepatic disease with hypoproteinemia	4	..	..	4	..
Cardiac insufficiency					
a. with hypertension	24	19	..	5	..
b. with hypotension	19	6	..	7	6
Parkinsonism	16	2	..	14	..
Tetany (hypoparathyroidism) with hypocalcemia	8	2	..	6	..
Autonomic nervous system lability					
a. normo-and hypotonic	11	4	..	7	..
b. hypertonic	18	15	..	3	..
Skin and hair changes					
a. gray hair	35	28	..	7	..
b. alopecia	18	3	..	15	..
c. senile skin changes	33	29	..	4	..

Procaine allergy has not been observed in the patients I treated. A procaine intolerance probably occurred in two female diabetic patients who were undergoing treatment with insulin. Both patients reacted to the procaine injection with biliary colics. A continuation of the injections resulted in the same type of reaction, for which reason the procaine treatment had to be abandoned.

In testing the efficiency of a drug associated with such therapeutic claims as Compound H_3, or procaine, it should be considered whether one is chiefly treating healthy elderly subjects or diseased persons. Testing such compounds in normal individuals is undoubtedly difficult, because no exact biometric age index is available. The situation with which one is confronted in the treatment of actual disease conditions is much simpler, because a clinical evaluation of the result of the treatment usually is possible. The objection can therefore be made that one is not dealing with a geriatric remedy but merely with an ordinary pharmaceutical compound. I am in agreement with this latter point of view, because both Aslan and all subsequent investigators, with the exception of Móra (10), have expressed the same opinion.

The usual laboratory tests were made on all the patients; these tests showed no significant changes during the procaine therapy which could be ascribed to the drug. In particular, no changes were observed in the blood picture, the erythrocyte sedimentation rate, or the serum lipid values, nor did any alterations occur in the serum protein fractions, as claimed by Aslan (2). The serum concentrations of calcium, phosphorus, and PBI also remained unchanged. In those patients in whom the X-ray examination had revealed signs of aortic arteriosclerosis, no certain changes were noted in the roentgenograms taken at the end of the therapy. In those patients in whom an arcus senilis of the cornea was present, a regression

of this pathological condition did not occur. Likewise the tortuosity of visible arteriosclerotic arteries remained unchanged.

Significant changes were, however, observed in one area in which one might not have expected it. These observations are listed in table 2 as the item of skin and hair changes. Aslan mentioned an eutrophic effect of procaine on the skin and its appendages. This statement is, however, only partly correct, since in general only the skin but not always the hair responds to the therapy. The yellowish, paperthin, flaccid senile skin becomes tight, regains its turgor, and becomes smooth, so that the patients look younger than before. This effect may be the only demonstrable result of the procaine therapy, as I have pointed out previously (9, 10). It makes, however, a remarkable impression when arthritic patients, who show practically no improvement in their main disease, suddenly present a rejuvenated appearance. With regard to the hair, it should be mentioned that in some patients after 10-15 injections a repigmentation of their grey hair occurs. This has been confirmed by other physicians too who usually, when their hair turns grey again, take a procaine treatment (generally one or two series each year). The situation concerning the effect of procaine on premature baldness is, however, quite different, even though such effect has been claimed by Aslan (2) and especially Schölzel (14). In the present study only such patients were included who did not have cicatricial changes in the scalp. If seborrhea was present, a mild antiseborrheic drug was employed. Patients with alopecia have usually suffered from that condition for many years and have tried a variety of drugs.

In my patients, improvement of the alopecia was observed in only three patients, and hair growth in these patients was only moderate. In these subjects procaine was used in combination with bee honey (Preparation Prokopin "G") (10), because bee honey has a composition somewhat similar to that of acetylcholine (9, 11) and because it has been claimed, especially by Japanese investigators (15), that acetylcholine has an effect on hair growth. In spite of occasional acetylcholine injections directly into the scalp, only negative results were observed, except in the three cases mentioned. Procaine, in the author's opinion, does not offer any greater chance or any smaller chance of correction of alopecia than any other hair growth remedy.

Similarly discouraging was the effect of the procaine treatment in patients with Parkinsonism. Only two such cases with unilateral tremor showed any improvement. In the other patients, no effect was observed, in spite of the fact that these patients were particularly eager to adhere closely to the injection schedule. No therapeutic effect was noted either in patients with arthrosis or arthritis. In acute arthritis the procaine therapy is in itself not recommendable. Each patient insists on receiving additional analgetic and antirheumatic drugs to alleviate the pain and is therefore not content with receiving three procaine injections weekly. In patients with chronic arthritis a subjective improvement was encountered in only a small percentage of the cases, so that in general the procaine therapy cannot be recommended in this disease category.

The therapeutic failure of procaine treatment in patients with bronchial asthma is somewhat surprising, because the drug theoretically would be expected to be effective in this condition. Thus, there exists a series of antiasthmatic drugs which contain procaine (in Germany: Asthmocain, Novocajod). The reported two cases of improvement represent young patients who were just above 20 years of age.

Positive effects can be ascribed to procaine in the treatment of symptoms associated with arteriosclerosis, but with regard to arteriosclerosis one has to be especially cautious in the evaluation of the effect of the drug, because of the difficulties associated with the diagnosis of arteriosclerosis. A subjective improvement was recorded in most of the cases; thus, headache, tiredness, and auditory noises showed a tendency to decrease and the physical strength of the patients and their interest in their work increased. Equally favorable was the effect of procaine in patients with cerebral arteriosclerosis. Patients with severe dementia or psychotic individuals were, however, not included in the study. It is of interest to note that two other authors (4, 6) have reported an improvement in hearing as the result of the procaine therapy. In addition, Móra (12) has been able to record improvements in neurologic-psychiatric tests.

Less surprising is the observation that the cardiovascular system responded to procaine administration; this beneficial effect of procaine on conditions of cardiac arrhythmia is well known in the field of cardiac surgery. In addi-

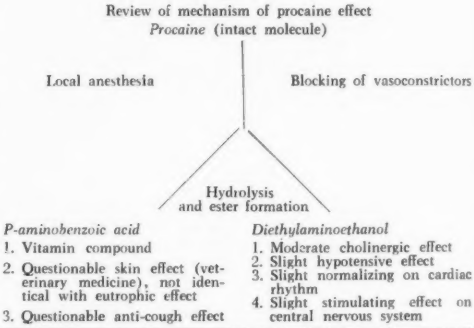
tion, procaine generally is in some cases able to normalize conditions of tachycardia. With regard to hypertension, the effect of procaine was particularly valuable in patients with labile hypertension. Cases with stabilized hypertension also responded, however, so that it can be recommended that hypertensive patients be given a preliminary procaine therapy before the administration of ganglionic blocking drugs. It should be emphasized that the patients included in the present study did not receive any cardiac drugs, nor were they immobilized through bed rest.

Before the present review was written, the patients were reexamined. The results of these examinations are reported in table 3. It will be seen that, in the patients who responded positively to the procaine treatment, the effect usually had subsided after 5 months and at the latest after 7 months. In some of these patients a second series of treatment consisting of 48 injections was then given. The results, listed in table 4, are particularly interesting because they show that a certain number of the patients who had reacted positively to the first treatment did not respond to the second series of procaine injections. With regard to those patients in whom a favorable effect again occurred, the effect took place later and was less pronounced than during the first treatment. Móra (12) seems to have arrived at similar conclusions with regard to this point.

The reported observations require an interpretation of the nature of the procaine effect.

Figure 1

Review of mechanism of procaine effect


Procaine (intact molecule)
Local anesthesia
Blocking of vasoconstrictors
Hydrolysis and ester formation
P-aminobenzoic acid
1. Vitamin compound
2. Questionable skin effect (veterinary medicine), not identical with eutrophic effect
3. Questionable anti-cough effect
Diethylaminoethanol
1. Moderate cholinergic effect
2. Slight hypotensive effect
3. Slight normalizing on cardiac rhythm
4. Slight stimulating effect on central nervous system

In this connection, however, the mechanism of the procaine action will not be discussed, nor will a review be made of the problem of whether the intact procaine molecule or the compounds released through its disintegration are responsible for the effect. This matter has been discussed in other publications (9, 11). Aslan (3) places emphasis on the vitamin nature of procaine, whereas the present author (9) directs attention to similarity between procaine and the metabolism of acetylcholine.

It should further be considered why the various preparations listed in table 1 in general have proved equally effective. In order to make a better comparison, I have further summarized my experiences with other geriatric drugs which do not contain procaine. All the geriatric drugs which proved to be of therapeutic value in general exhibited effects similar to those observed during treatment with procaine. As seen from table 5, quite different compounds were being considered in this respect.

With regard to acetylcholine, I have in one instance given intramuscular injections of pure acetylcholine in doses of 100 to 200 mg. three times weekly, according to a schedule similar to that used in the procaine therapy. I had not anticipated any great effect, because the decomposition of acetylcholine through the action of acetylcholine esterase probably proceeds at a

Table 3. Review of Duration of Procaine Effect Based on Follow-up Study of 111 Patients.

Duration of Effect (Months)	Number of Cases
1	3
2	12
3	6
4	21
5	39
6	14
7	3
8	5
9	2
10	4
11	0
12	2

Table 4. Effect of Second Series of Treatment with Procaine in Patients Who Responded Favorably to First Series of Procaine Injections.

Number of Cases	Objective Improvement	Subjective Improvement	No Effect	Aggravation of Condition
63	27	8	20	8

Table 5. Effect of Treatment with Various Procaine-free Geriatric Preparations.

Preparation	Number of Cases	Improvement	No Improvement
Acetylcholine	13	5	8
Vitamin B_{12} (+ Vitamin C)	53	44	9
Strychnine	10	6	4
2-(p-Aminobenzo-sulfonamido)-pyrimidine	8	3	5

faster rate than the decomposition of procaine. The results of the treatment nevertheless showed a marked similarity with those exhibited by procaine. The acetylcholine powder was dissolved in water immediately before the injection, in the presence of the patient, who therefore realized that a special drug was being administered.

As a second geriatric drug I have given intramuscular injections of vitamin B_{12} in combination with vitamin C two or three times weekly. During the first week 2.5 mg. of B_{12} and 100 mg. of vitamin C were given in each injection; subsequently, only 1.0 mg. of B_{12} and 50 mg. of vitamin C were administered. The B_{12} treatment also proved very satisfactory, so that such therapy can now be recommended as a general geriatric treatment. Also in the case of this drug, however, there were some patients who did not show any response to the therapy. With regard to the effect of vitamin B_{12}, this can probably be characterized as a genuine pharmacological effect.

As a third drug, 10 mg. of the sodium salt of strychnine were given intramuscularly every second or third day for a period of three weeks. Because of the possible danger of a cumulative intoxication, the treatment was only continued for a period of three weeks. Also in the case of this drug the effects were similar to those observed with the treatment of procaine.

In general the effect of the drugs listed in table 5 was similar to that of procaine and consisted of relief of tiredness and an increase in vitality; even a beneficial effect on the skin was occasionally observed, and the patients' psychic condition was usually improved.

The question arises whether the observed effect of these drugs may not be connected with an improvement in the psychological condition of the patient, to which those persons who are in possession of mobilizable reserves respond with symptoms of revitalization.

In the Aslan type of procaine therapy we undoubtedly have to consider two factors which are responsible for the effect. The purely pharmacodynamic factor, which is illustrated schematically in figure 1 (9) would not be sufficient to explain the definite positive responses. A strong psychological factor must also be included, which probably is especially intensified through the sensational newspaper reports. As an explanation of the unusually favorable results observed by Aslan, one should most likely also take into consideration the fact that patients admitted to the clinical department of the Geriatric Institute in Bucharest receive excellent care there.

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BOOK REVIEWS

DIE ALTERSVERÄNDERUNGEN DER HALSWIRBELSÄULE (Aging Changes in the Cervical Spine) by Ulrich Ecklin, Springer-Verlag. Berlin-Göttingen-Heidelberg, 1960, 81 pages, paper bound, DM 28.

The primary purpose of this study of 140 human cervical spines obtained from fetuses and individuals of various ages was to compare the life history of the cervical segment with that of the remainder of the spine. The changes in the spine occurring with age are believed to be largely in the intervertebral discs. While certain phases of development and aging of the latter take a similar course in different parts of the spine, the life history of the cervical spine is related to the fate of the uncinate processes, which are lacking in the thoracic, dorsal, and lumbar segments. From late childhood on the surface of the uncinate processes become involved in the formation of joint-like structures, the so-called uncocervical joints. These cavities, which are traced back to tears in the intervertebral disc, are supposed to result from functional stress and to occur in previously healthy tissue. These cracks become organized by fibrous tissue undergoing cartilagination and, in due course of time, they may be involved in senile osteoarthrosis.

The data are well documented by numerous illustrations, gross and x-ray pictures, and photomicrographs. There seems to be considerable overlapping of the findings at different ages and in various vertebrae. However, there are no statements indicating the degree of overlapping or what findings should be expected in the majority of individuals at certain age groups. No sex differences are mentioned.

In this primarily anatomical study the histogenetic mechanism of neither age changes nor the evolution of osteoarthrosis is dealt with, nor was an attempt made to correlate the findings to osteoporosis or Paget-like lesions of the spine. It would also have been desirable to correlate the observations to some work done on the histochemistry and cytology of the intervertebral discs, especially because of the author's opinion that "fundamentally one has to distinguish sharply between degenerative regressive changes affecting cells as opposed to aging processes which originate in the intercellular substance." This view will hardly be shared by the majority of cytologists. Most clinicians on the other hand, will take exception to the statement that only rarely do advanced aging processes in the spine lead to clinical symptoms. These are some of the many questions that can be raised when reading this report; they should, however, not detract from the value of the careful and detailed observations laid down in this monograph.

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"H3" IN THE BATTLE AGAINST OLD AGE, by Henry Marx, Plenum Press, Inc., New York, 1960, 207 pages, $4.95.

This volume is of no use to the physician and its value to the lay public is very questionable. It is primarily based on the publications of Dr. Anna Aslan. These, under the title of "Research on Novocaine Therapy in Old Age," have been reviewed in the JOURNAL OF GERONTOLOGY. It was pointed out in that review that it is impossible to explain the results claimed by Dr. Aslan and her coworkers on a biochemical or pharmacological basis. Publication of the present volume did not change this reviewer's opinion. Publication of books of this kind will have two consequences: 1. Raise false hopes in the aged and sick, 2. Give the opportunity to unscrupulous practitioners of medicine for the finannancial exploitation of gullible individuals by the prolonged repeated administration of injections. The work of Dr. Aslan should be repeated under strictly contolled circumstances on a large number of subjects to settle once and for all the validity of her claims.

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Pittsburgh, Pennsylvania

BOOKS RECEIVED

GERIATRIC NURSING, by Kathleen Newton, 3rd edition, C. V. Mosby Co., St. Louis, 483 pages, 1960, $6.50.

MENTAL DISEASE AMONG JEWS IN NEW YORK STATE, by Benjamin Malzberg, Intercontinental Medical Book Corporation, New York, 1960, 140 pages, $3.75.

RESEARCH HIGHLIGHTS IN AGING, A SELECTION OF SCIENTIFIC PAPERS ON RESEARCH IN AGING CARRIED OUT OR SUPPORTED BY THE NATIONAL INSTITUTES HEALTH IN 1959, Public Health Service Publication No. 779, prepared by Robert W. Palmer and the Center for Aging Research, Division of General Medical Sciences, National Institutes of Health, Superintendent of Documents, U. S. Government Printing Office, Washington, D. C., 52 pages, paper bound, 25 cents.

STRIKE BACK AT ARTHRITIS, Public Health Service publication No. 747, Superintendent of Documents, U. S. Government Printing Office, Washington, D. C., 45 pages, paper bound, 40 cents.

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Section B

Psychological and Social Sciences, Social Welfare

Edited by

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Bernice L. Neugarten, Ph.D.

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VOLUME 15, SECTION B OCTOBER, 1960 NUMBER 4

AGING AND THE DECLINE OF INSTRUMENTALITY

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What are the attitudes of the middle-aged, the aging, and the aged toward age itself? Or, more precisely, how are people over fifty oriented toward the positions they currently occupy in the life cycle? Do these orientations shift, from one decade to the next? If so, what is the nature of the shift?

In their most general form, these are the questions with which we are concerned in this research report. The data, drawn from the Kansas City Study of Adult Life, a social-psychological study of the aging process,[1] consist of responses from about 200 men and women aged fifty to ninety to the questions: "What are the best things about being the age you are now?" and "What are the worst things about being the age you are now?" Since these were not asked as closed-category questions based on precise hypotheses, we examined and classified the free responses, after the fact, according to a scheme deriving from the general distinction between "instrumental" and "integrative" (or "expressive") orientations to self-in-society (Parsons & Shils, 1953). We then examined the relationships between these "orientations to age" and chronological age, employing in this first approximation no control by sex, social class, or other background factors.

Broadly speaking, in response to the first ("best things") question, there is an apparent shift with age toward the integrative-expressive orientation, a shift that is consonant with the Kansas City Study's more general "disengagement" theory of aging (Cumming, Dean, Newell, & McCaffrey, 1960). There is, furthermore, in response to the second ("worst things") question, a shift with age from anxiety in the integrative-expressive area to frustration in the instrumental area.

[1] The Kansas City Study of Adult Life is financed by Grant 3M-9082 from the National Institute of Mental Health to the Committee on Human Development of the University of Chicago. It is under the supervision of William E. Henry (Principal Investigator), Robert J. Havighurst, and Bernice L. Neugarten. The Study Director has been Elaine Cumming, and the Field Director, Lois R. Dean.

Before presenting these findings in greater detail, we will attempt in the two sections to follow to clarify (1) the disengagement theory, and (2) the instrumental-integrative distinction that constitutes the framework for this analysis.

THE DISENGAGEMENT HYPOTHESIS

The intent of the Kansas City Study of Adult Life has been to develop hypotheses about social-psychological changes occurring during the process of "normal" aging that can be directly attributed to age change alone, rather than to such age-related but peripheral variables as reduced economic circumstances, retirement, or loss of children from the home. A research design has been employed whereby, since 1956, we have periodically interviewed a panel of some 140 working and middle-class Kansas Citians in transit from middle to old age (their ages at selection ranged from 49 to 69). Since "normal" aging is the focus, the panel members are ambulatory and self-sufficient in the community; none is institutionalized, indigent, or severely handicapped either physically or mentally. To this basic study panel, a group of similarly healthy and ambulatory people in their seventies and eighties was subsequently added.

Quite early in the research, by comparing the 80-year-olds with middle-aged panel members, we began to develop the concept of "disengagement" as the major social-psychological dimension along which change in the latter part of the life span occurs. To summarize briefly: By "disengagement" we mean a process whereby people become extricated with age from the close, obligatory interactions of middle life. Disengagement has been tentatively posited as an emergent as well as a responsive phenomenon, and its major concomitants are: (1) a reduction in amount, variety, and intensity of social interaction; (2) a release, therefore, from

many of the normative controls governing social interaction; (3) a shift in orientation to social interaction that includes a movement away from primarily instrumental to primarily integrative-expressive orientations to the social environment. It is with this third aspect of disengagement theory that this report is concerned.

THE ANALYTIC CATEGORIES

In the words of Talcott Parsons and Robert F. Bales:

> The instrumental-expressive distinction we interpret as essentially the differentiation of function, and hence of relative influence, in terms of the "external" vs. "internal" functions of the system. The area of instrumental function concerns relations of the system to its situation outside the system, to meeting the adaptive requirements of its maintenance of equilibrium, and "instrumentally" establishing the desired relations to *external* goal-objects. The expressive area concerns the "internal" affairs of the system, the maintenance of integrative relations between the members, and regulation of the patterns and tension levels of its component units (Parsons & Bales, 1955).

Parsons and Bales apply the instrumental-expressive distinction to the *social* system (specifically, in the work cited, to the role structure of the nuclear family). We apply the distinction here to the *personality* system (Parsons, 1956)—or, more concretely, to the differential orientations of *individuals* to the external environment. In this context, then, we have modified the above definition to read:

> The instrumental orientation focuses on relations of the individual to his *exterior* situation, to meeting the adaptive requirements for maintaining equilibrium with the social environment, and instrumentally establishing the desired relations to *external goals*. The expressive, or integrative, orientation focuses on relations of the individual to his *interior* situation, to meeting the integrative requirements for maintaining psycho-biological equilibrium, and to regulating the patterns and tension levels associated with *internal needs*.

Within this broad frame of reference, we developed eight empirical categories, four serving to classify responses to the "best things" question, the other four representing the obverse of these and serving to classify responses to the "worst things" question. Two of these four pairs can be directly identified with the instrumental and integrative polarities; one represents a mid-point on the continuum; and the fourth is a residual category containing responses that deny the validity of the questions. The categories, including in each case some representative statements from respondents, are these:

I. Responses to the question: "What are the best things about being the age you are now?"

A. *Output:* Responses emphasize active engagement in the social environment, with focus on achievement, responsibility, power and influence, utility, knowledge, experience.

e.g.—"My ability to use the things I've observed and learned from experience."
"My work. If you keep both mind and body busy, it is easier. You know there is something required of you."
"In the type of work I do, people pay more attention to me now. They feel I know what I'm doing. I'm in a position to help my friends make some money."

B. *Intake:* Responses emphasize active engagement in the social environment, but with focus on freedom, enjoyment, immediate gratification, contemplation, "wisdom" for its own sake.

e.g.—"The children have grown up and I have grandchildren. They have the responsibility and I have the fun."
"I'm more relaxed about living. Now I don't care what others think. I feel so free. I am perfectly happy here in the house, reading and watching TV."
"You are your own boss. I do just as I please. I can go to town if I want to, and I don't have to ask anybody."

C. *Survival:* Responses reflect a passive relationship to the social environment, with emphasis on conservation of resources (biological, psychological, economic). The social environment is merely a backdrop, if present at all, in these responses.

e.g.—"I think I'm doing fine at my age. I can hear. I can't see too good, but I can crochet."
"Being alive. Being able to eat and sleep. Awfully hearty eater. Eat all the time."
"To have the feeling of contentment and to have your needs fulfilled."

D. *Denial-Rejection:* There is "nothing good" about present age; or, "I don't think of myself as any special age."

e.g.—"The best thing is that I'm not any *older*."
"I don't think of myself as any particular age. I don't feel any different than 34 or 44."

II. Responses to the question: "What are the worst things about being the age you are now?"

A. *Frustrated Output:* The obverse of "A" above. Responses emphasize loss of ability to "do," to achieve, to assume responsibility; loss of respect from others. This category includes responses about physical weakening, if this weakening is seen primarily as interfering with "doing."

e.g.—"It makes you realize you are getting older and can accomplish less. I can't cope with tension and turmoil."
"Looking back and realizing that I didn't take advantage of all the opportunities

I've had. Instead of having the money I have, I could have had three times as much."
"Not being able to work. I still like to work, but I can't get a job."

B. *Frustrated Intake:* The obverse of "B" above. Responses emphasize loss of means or capacity to enjoy; loss or absence of freedom from responsibility; loss of friends, family, companionship; loss of "looks."
e.g.—"I can't get out at night and do the concerts and things."
"Getting wrinkles. And knowing I won't be able to keep on playing golf so much longer."
"Friends that are dying, and the sickness that is attacking a lot of them."

C. *Threatened Survival:* Responses emphasize threats to health and welfare for their own sake. "Just getting old." Death fears.
e.g.—"My memory is slipping. I don't remember where I put things."
"You realize you don't have as many years ahead of you. You have to admit that, but you don't like to think about it."
"Aches and pains and ailments. Something new every day."

D. *Affirmation-Acceptance:* There is "nothing bad" about present age.
e.g.—"Not any worst thing. I don't fight growing old. I'm doing my best to be a graceful old man."
"I don't know, I take life as it comes. I wouldn't want to go back. Life is pleasant now."

In ideal-typical terms, the "output" categories embrace an instrumental orientation; the "survival" categories embrace an integrative-expressive orientation; and the "intake" categories embrace what might be termed a quasi-integrative orientation, since they are focused on the social environment, but place principal emphasis on sensual gratifications and absence of responsibility for others.

As a first step toward determining the reliability of these categories, another sociologist not associated with the Kansas City study of Adult Life[2] classified a random 50 cases, using only the definitions enumerated above. For those categories based on the "best things" item, 84 per cent agreement with the author's judgments was obtained; for the categories based on the "worst things" item, 89 per cent agreement was obtained.

FINDINGS

First of all, it is perhaps surprising that, as shown in Table 1, fewer than 20 per cent volunteered denial or rejection of aging. Clearly, the modal orientation toward the rewards of advancing age is the "intake" or quasi-integrative, while the modal orientations toward the punishments of advancing age are the blocked instrumentality and the purely integrative (survival) orientations. The respondents, in short, appear to aspire to the best of both worlds, i.e., instrumentality without responsibility. Few among those complaining of diminishing instrumentality mention gainful employment, for example, and almost none indicate a desire to take more responsibility for their families. Instead, the typical response in this category emphasizes loss of the physical capacity to "do," in a very general sense. This finding is in accord with the disengagement hypothesis, which predicts increasing disenchantment with obligatory activities and interactions.

Table 2 shows a sharp decline in the instrumental orientation (output) from the 50's through the 80's, with the major shift at about age 60. Even more dramatic is the increase in the purely integrative orientation (survival), with the major shift at about age 70. Denial or rejection of advancing age diminishes with age, the shift occurring at about age 60. Only the respondents in their 50's appear resentful in any significant numbers toward the aging or aged status, suggesting that, as with many feared conditions, anticipation is worse than the condition itself. Finally, this table shows an

TABLE 1. RESPONSES TO "BEST THINGS" AND "WORST THINGS" QUESTIONS: FOR ALL RESPONDENTS (PERCENTAGES).

	"Best Things" ($N=207$)		"Worst Things" ($N=205$)
A. Output	17	A. Frustrated Output	38
B. Intake	41	B. Frustrated Intake	12
C. Survival	24	C. Threatened Survival	39
D. Denial-Rejection	18	D. Affirmation-Acceptance	11

TABLE 2. RESPONSES TO "BEST THINGS" QUESTION: BY AGE (PERCENTAGES; $N = 207$).

	Age Group			
	50–59 ($N=60$)	60–69 ($N=51$)	70–79 ($N=66$)	80+ ($N=30$)
A. Output	37	16	6	3
B. Intake	28	59	41	37
C. Survival	2	14	41	47
D. Denial-Rejection	33	11	12	13

NOTE.—This distribution is significant beyond the .001 level ($X^2 = 67.73$).

[2] The author is indebted to Dr. Warren E. Kalbach of Portland State College for his assistance in this preliminary reliability check.

upsurge in the quasi-integrative (intake) category among the 60-to-70-year-olds, and a decline in this orientation in the older groups.

As shown in Table 3, on the other hand, the younger respondents, complaining of "aches and pains," are more oriented to survival, the purely integrative category, than are the older respondents. The 70-and-80-year-olds show preoccupation with instrumentality (frustrated output) and complain of inability to control the environment, of incapacity to "do" for themselves and others.

We can offer only the most general and speculative interpretations for the relationships that appear in Tables 2 and 3. The major shift in orientation to age on the reward side, from focus on instrumentality to focus on psychobiological integration, or survival, we interpret as further evidence in support of the disengagement hypothesis. These responses may be viewed as the psychological aspect of disengagement from society; the subjective manifestations of the weakened body and shrunken lifespace of the old in our culture. From the viewpoint of the disengagement hypothesis, this decline with age in orientation to instrumentality is consonant with shifts we have found in orientation to interaction, with diminished affect and reduced concern with interaction of any kind, and with increasing preference for a small lifespace.

The upsurge in the 60's of the quasi-integrative orientation, the "freedom-enjoyment" theme, is perhaps related to the fact that this is the decade of retirement from work, maturity and independence of offspring, and the development of grandchildren into amusing playthings. These are the years, in short, of extrication from the large responsibilities of young adulthood and middle age; and mind and body, for the most part, retain the capacity to enjoy this "new birth of freedom." The typical 65-year-old can come and go as he pleases, and does not yet bear the full burden of a failing body. He is free, provided he has the financial means, to focus on non-obligatory, maximally enjoyable activities and interactions.

As for Table 3, the punishments of advancing age, it seems probable that the middle-aged and aging (50- and 60-year-olds) focus heavily on the survival theme because, for the first time, they are experiencing "aches and pains" of more than passing consequence. For most respondents in this age group, the stiffening joints constitute little more than an annoying interference with normal activities; but for some, physical deterioration spells genuine trauma (as, for example, in the case of one respondent whose heart attack in his early fifties shocked him into the recognition of mortality: "I always thought I was just practicing life and could go back and do it again," he said. "But since my heart attack, I've realized this is *it*, that's all there is.") The weakened body has probably not yet been incorporated into the self-image of the middle-aged and aging, and they may be anxious about it. It seems reasonable to suppose that the very old, on the other hand, have long since grown accustomed to physical incapacitation, so that this does not leap to the forefront of their minds as a "worst thing" about their age. Indeed, they count themselves fortunate that they are still among the living; hence the emphasis on survival as a "best thing" about their present age.

The expressed desire for greater instrumentality (i.e., the focus on frustrated instrumentality shown in Table 3) among the older respondents may be a function in part of their distance in time from concrete instrumental roles. It has been so long since these people have actually experienced the hard responsibilities of middle age that a halo may now surround these responsibilities, and they may no longer be perceived as burdensome. We know of no definitive check for this hypothesis, but responses to other questions suggest that it may have merit: that is, when asked about specific instrumental roles, these older respondents show little willingness to assume them. They reveal, for instance, an eagerness to return grandchildren to their parents after a few hours; a desire for visits and gifts from others, without obligations to them; a proneness for uttering lofty generalizations about how, for example, to solve the "youth problem," as contrasted with the far more specific-concrete solutions proposed by the middle-aged (who must

TABLE 3. RESPONSES TO "WORST THINGS" QUESTION: BY AGE (PERCENTAGES; $N = 205$).

	Age Group			
	50–59 (N=59)	60–69 (N=51)	70–79 (N=66)	80+ (N=29)
A. Frustrated Output	22	31	53	48
B. Frustrated Intake	19	14	3	17
C. Threatened Survival	44	41	38	24
D. Affirmation-Acceptance	15	14	6	10

NOTE.—This distribution is significant beyond the .05 level ($X^2 = 19.22$).

actually deal with the problem); a comparatively low concern with interaction of any kind, and a rejection of the specific and neutral orientations to interaction (the instrumental orientations of work and the marketplace).

Still another possibility in this connection is, of course, that our older respondents are responding normatively to this question. They may, in other words, be conforming their responses to a belief that society expects old people to deplore the loss of instrumentality, or social "usefulness," and does not expect them to sit back and watch the rest of the world go by, as so many indicate a desire to do.

SUMMARY

Preliminary analysis of two open-end questionnaire items dealing with the rewards and punishments associated with growing old, as these are perceived by a sample of 200 middle- and working-class men and women aged 50 to 85, strongly suggests the following:

1. Resistance, expressed as direct rejection of the aging or aged status in general, or indirectly as denial of the respondent's specific age at present, is low and it diminishes with increasing age.

2. Orientation to instrumental roles as a reward of aging declines with age, while the integrative-expressive and "quasi-integrative" reward orientations increase with age.

3. As a punishment associated with aging, threatened psycho-biological integration (survival anxiety) diminishes with age; while expressions of frustrated instrumentality increase with age.

We interpret these tentative findings as support for the general theory of *disengagement from social obligation* as the major social-psychological dimension along which change in the latter part of the life span occurs.

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FAMILY RESPONSIBILITY AND THE HEALTH OF OLDER PEOPLE*

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There is a widely-held popular belief that affectional and other ties between older people and their families are weaker now than they were at the turn of the century or at other times in the past. This belief flourishes not only in the United States but also in the industrialized countries of western Europe. In this country the alienation of older people from their families has become one of the descriptive items about the aged often taken for granted. Since there are no empirical studies of the relationships of older people and their families which date back to the "good old days" of the nineteenth century, it is difficult to know just what the "true" situation was in that pre-sociological and pre-social-work time.

Empirical evidence is available, however, which indicates that the family ties between older people and their children are still strong and still functioning. The data presented in this paper reinforce the findings reported by Adams (1957), Brown (1960), Streib (1958), and Townsend (1957), among others. The point of view of these studies has been summarized by the World Health Organization in their evaluation of the situation of the elderly:

> . . . Wherever careful studies have been carried out in the industrialized countries, the lasting devotion of children for their parents has been amply demonstrated. The great majority of old people are in regular contact with their children, relatives, or friends. All the same, industrial and urban development increases social and geographical mobility, and a small portion of the aged are as a result left with few human contacts, particularly in large cities. . . . There is also a marginal group, a still larger number of aged people whose survival in the community is precarious and bought at the cost of hardship to relatives or friends.
>
> . . . A number of investigators have shown that the three-generation family is very much alive even in the heart of great cities, and that the human relationships which it fosters are preferred by a high proportion of young people no less than old ones. Where distance permits, the generations continue to shoulder their traditional obligations, of the elders toward their children, and the children to the aged (World Health Organization, 1959, pp. 6, 7).

* A revised version of a paper presented at the National Health Forum, Miami Beach, Florida, March 16, 1960. Certain data from this paper were also presented at the Annual Meeting of the Trustees of the Health Information Foundation, New York, May 5, 1960.

SAMPLING

The present data are taken from a broad study of the health needs of older people made by the National Opinion Research Center of the University of Chicago under a grant from the Health Information Foundation. The sample was nation-wide and of the area-probability type. It resembled in general design that employed by the United States Census Bureau in the Current Population Survey (Hansen, Hurwitz, Nisselson, & Steinberg, 1955). Multistage sampling was used, and sampling procedures were developed so that every person aged 65 years and older who was not living in an institution had an equal chance of being located. A sample of 1,734 persons was interviewed in the spring of 1957.[1] Each person interviewed was asked to identify the individual, other than spouse, to whom he would turn in a health crisis. These near relatives and friends of the older people were located wherever they lived in the United States[2] and interviewed. It was not possible to interview about 4 per cent of all older people located in the preliminary screening because they or the persons taking care of them reported that they were "too sick." Interviews were held, however, with most of the individuals who were taking care of those older people who were too sick to be interviewed.

In the fall of 1957, additional interviews focused on the health needs of the aged were conducted with 2,507 persons aged 21 and over, comprising a cross-section of the adult American public. Material from each of these interview series—those with older people, those with responsible relatives, and those with the public cross-section—will be included in this paper.

FINDINGS

To simplify analysis, the major emphasis in this paper will be on the family situation of

[1] James S. Coleman, formerly of the Department of Sociology, University of Chicago, and the National Opinion Research Center, was responsible for the sample design in this investigation. Dr. Coleman is now Chairman, Department of Social Relations, Johns Hopkins University.

[2] This operation was possible because the National Opinion Research Center maintains a nation-wide interviewing staff.

only those older people who have living children. While there is evidence that the extended family plays an important part in the life of some older people who have never married or who have no children, these relationships with brothers, sisters, nephews, nieces, and others will not be considered here. Specifically, two topics will be discussed: first, the reported physical proximity of older parents and their children and the relation of the health of the older parents to such physical proximity; and second, the attitudes of persons toward suitable living arrangements for older parents.

Proximity of parents to children

Four of every five older persons interviewed (78 per cent of the total sample) said that they had living children (see Table 1). Thirty-six per cent of all persons with living children lived in the same household with at least one child; an additional 24 per cent, while they lived apart from their children, had at least one child who lived on the same block or within walking distance. Six of every ten persons with children, then, were within walking distance of at least one child.

Twenty-five per cent of the older population with children reported that their nearest child was a short ride away, and 15 per cent said their nearest child lived as far from them as a day's travel or more. Except for those persons whose nearest child lived a day's travel or more distant, almost every older person had seen at least one child within the week preceding the interview.

These materials on the physical proximity of parents and children show clearly that despite the much-discussed mobility of the American people, despite the movement from the country to the city and the transition from a rural to an urban environment, if an older person has children, in almost nine cases of every ten at least one child is apt to live no farther than a short ride away, and in six cases of every ten at least one child is within walking distance of an aged parent.

Further, the "sicker" the older person, the more likely he is to live in close proximity to one of his children. The health status and needs of older people differ greatly. Using self-reports of illness as a basis of estimation, the "very sick" group in the older population outside of institutions is estimated at between 10 and 14 per cent.[3] Four of every five of the "very sick" group interviewed reported that they had living chidren. As Table 1 shows, among the "very sick" with living children, 44 per cent lived in the same household with at least one child; an additional 27 per cent lived on the same block or within walking distance of at least one child. Seven of every 10 of the "very sick" were within walking distance of at least one child,[4] as compared with 6 of every 10 in the rest of the older population with children.

Other findings from this survey also indicate that as parental needs in the health area become greater, as nursing care or special diets

[3] The lower proportions are based only on those interviewed in the study; the higher proportions include those "too sick" to be interviewed but located in the non-institutional population.

[4] The number of "very sick" with children is small. Data are therefore subject to considerable sampling variation.

TABLE 1. LOCATION OF NEAREST CHILD OF ALL PERSONS AGED 65 AND OVER WHO REPORT LIVING CHILDREN: BY DEGREE OF ILLNESS OF THE OLDER PERSON[a].

Location of nearest child	Percentage distribution								
	Total			"The Very Sick"			"All Others"		
	Total	Men	Women	Total	Men	Women	Total	Men	Women
Total[b]	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
A child in household with older person	36.1	32.2	39.7	44.4	35.3	49.5	35.2	31.9	38.2
Nearest child in same block	11.6	11.8	11.5	15.3	19.6	12.9	11.2	11.1	11.3
Nearest child within walking distance	12.1	13.5	10.9	11.8	13.7	10.8	12.2	13.5	11.0
Nearest child a short ride away	25.0	25.3	24.7	20.1	23.5	18.3	25.5	25.4	25.6
Nearest child within a day's travel or more	14.6	16.6	12.8	8.3	7.8	8.6	15.3	17.4	13.4
No answer	0.5	0.6	0.4				0.6	0.7	0.5
N =	1,350	637	713	144	51	93	1,206	586	620

[a] Non-institutional population only. Data subject to sampling variation.

[b] Proportion of sample who report living children: total, 77.9; men, 79.5; women, 76.4. Number who report living children: total, 1,350; men, 637; women, 713.

are needed, or as household chores become burdensome for the older person, the majority of children assume these responsibilities.

Attitudes toward living arrangements

Many factors enter into the decision of parents and children to set up a multi-generational household. Some of these factors have been suggested already—widowhood and ill health on the part of the parent. There is further information in this survey on the attitudes of older people and their children toward multi-generational living in the event of parental widowhood and ill health.

Both older people with children and their responsible relatives, who are primarily children, recognize that there are potential or existing areas of conflict between different generations living in the same house. The mother who says, "Of course I'd never dream of imposing on my children," and the child who says, "I'd do *anything* for my parents," do exist, but it takes very little insight to realize that these are superficial statements of attitudes which may cloak a variety of feelings. Beneath these "expected" responses, both older people and their adult children make much more realistic assessments of parent-child relationships. As an illustration, 76 per cent of the older people with children and 86 per cent of the responsible relatives of these older people agree that "lots of people who share a home with their children feel that their children don't really pay any attention to their advice."

Both older parents and their responsible relatives agree that the most desirable place for older people to live is in their own homes. Both parents and children feel that the least desirable place for older people to live is in a home for the aged or in an institution. A joint household with children, then, is considered a desirable place to live only if a home of one's own is not possible for the aged individual. These beliefs about where older people should live must be considered in juxtaposition with the facts given above: 44 per cent of the "very sick" who have children, and 35 per cent of the remainder of the older population with children, live in the same house with at least one child.

Attitudes of older people and their relatives. A number of case-questions dealing with various aspects of parent-child relationships were asked independently of older people with children and of their responsible relatives, who were largely children. One of these questions is given here. It focuses on a decision about family living which has an impact on three generations. It was a very real question for the respondents, some of whom had already faced comparable situations.

Tom and Mary Jenkins have four children. They live in a new section in a small three-bedroom house, and it gets pretty crowded. Mary's mother, Mrs. Stevens, is a widow, with a very small pension, and her health is poor. The doctor doesn't think Mrs. Stevens should live alone. He says that she doesn't need any special nursing care, just someone to keep an eye on her. What do you think Mary should do?

Despite the obstacles to three-generation living in the question—the small, crowded house, the bad health and poor financial status of Mary's mother—almost half of all older people with children (44 per cent) and almost half of the group of responsible relatives (47 per cent) said that Mary should move her mother into Mary's home. At the other extreme, 10 per cent of these older people and 11 per cent of these responsible relatives felt that Mary's mother should move to a nursing home or an institution. The remainder of the respondents had other suggestions for Mary and her mother; most of these were schemes whereby Mary's mother could continue to live in her own home, by moving closer to Mary or by living with a companion.

Attitudes of the public. Early in the interview the public cross-section was asked, "As you know, many older people share a home with their grown children. Do you think that this is generally a good idea or a bad idea?" Sixty-four per cent of the public felt that this was a bad idea.

Later the public cross-section was asked the question about Mary and her mother. Forty-five per cent of the public felt that Mary should move her mother in with her; 17 per cent said that Mary should place her mother in a home or an institution.

In order to bring Mary's situation a little closer to the experience of the public cross-section, these respondents, after they had told the interviewer what Mary *should* do, were asked, "What do you think Mary *really* will do?" Face-to-face with a more "real" Mary, 62 per cent of the public said that Mary would move her mother in with her; only 10 per cent said that Mary would place her mother in a home for the aged or in an institution.

Obviously, a large part of the American public, like a substantial portion of all older people

with children, and a substantial portion of the children of older people, feel that even if a joint household must be the result, the parental need for increased health care is a responsibility which must be assumed by adult children.

SUMMARY

There is a minority group of older people—about 22 per cent—who have no children. The special problems of these older people have not been treated here.

More than one-third of those older people who have living children are in a household with at least one child. Older people who do not live under the same roof as their children are not physically abandoned; on the contrary, most such older people live close to at least one child and see him often.

The poorer the health of the older person, the more likely he is to be living in the same household as an adult child. Whether this is a good or bad thing for parents and children cannot be answered categorically. Each such family situation must be analyzed in terms of its unique characteristics and the personalities involved.

The data indicate that, when confronted with parental health problems, children assume the obligations which are traditionally associated with the relationships of aged parents and adult children.

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PERCEPTION OF PART-WHOLE RELATIONSHIPS IN MIDDLE AND OLD AGE*

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An earlier study dealt with ontogenetic changes in perception of part-whole relationships that occur between 6 and 20 years of age (Wapner & Werner, 1957; Werner & Wapner, 1956). These changes in part-whole relations were studied by means of two kinds of illusions, the Müller-Lyer illusion based on assimilation of parts to the whole (Figure 1) and the Titchener Circles illusion based on a contrast relationship between parts (Figure 3). The following ontogenetic changes were found: (1) Between 6 and 15 years of age there is a decrease in susceptibility to the Müller-Lyer illusion, followed by an increase through 19 years of age. (2) There is an ontogenetic increase in susceptibility to the Titchener Circles illusion from 6 through 19 years of age. Aside from the increase in susceptibility to the Müller-Lyer illusion during adolescence, the ontogenetic changes in the two illusions are consonant with the developmental law which states that there is increasing differentiation and hierarchic integration with development. The Müller-Lyer illusion, due to embeddedness of parts within the whole (assimilation), in general, has greater effects with the youngest children; the Titchener Circles illusion, which requires an articulated relationship between parts (contrast), has greater effects at the later age levels.

The present study was directed toward the problem of determining the course of the changes in perception of part-whole relations, as reflected in these illusions, that occur beyond the 20-year level and in particular in old age. (The need for studies of this kind was pointed out by Braun [1959] in his review of research on perceptual processes in aging.) Its further purpose was to compare these changes with those obtaining at younger age levels so that the developmental changes from 6 through 80 years of age can be assessed.

The subjects of this study were 100 men between the ages of 20 and 80, divided into seven age groups. There were 10 subjects in each of the age groups 20-24, 25-29, 30-34, 35-39; and 20 subjects in each of three groups 40-44, 45-49, and 65-80. The *S*s between the ages 20 and 50 were drawn from the Clark University Evening College and the local community; those between 65 and 80 years were drawn from a community old-age club.

MÜLLER-LYER ILLUSION

Procedure. The Müller-Lyer pattern was presented as pictured in Figure 1. *S*'s task was to shorten the right part to apparent equality with the left part. The left part of the pattern (angles inward), 75 mm. long, was used as the standard; the right part, the variable, could be adjusted by using a rack and gear device. *S*, sitting 3 ft. from the pattern, adjusted the variable by turning a knob. Four trials were employed: on two trials the initial setting of the variable was small (25 mm.); on the remaining two trials it was large (125 mm.). The sequence of trials defined in terms of initial setting was the same for all *S*s, namely, small, large, large, small.

The mean difference (standard minus variable) served as the measure used in the analysis. Thus greater susceptibility is indicated by larger numbers.

Results. The results are presented in Figure 2, which shows the magnitude of the illusion (standard minus variable) for the various age levels. The graph indicates that, in general, between 20 and 39 years of age, susceptibility to the illusion remains fairly constant; beyond 39 years of age there is an increase in the illusion effect which is most striking in the 40-44 year age group.

The difference between age groups was evaluated statistically by analysis of variance. The source of variation between age groups (*MS* is 75.83 for 6 *df*), tested against the variation within age groups (*MS* is 29.96 for 93 *df*), was significant ($P < .05$). Table 1 shows the means (standard minus variable) for the various age groups. As indicated in Table 1, there are no

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Fig. 1. The Müller-Lyer pattern.

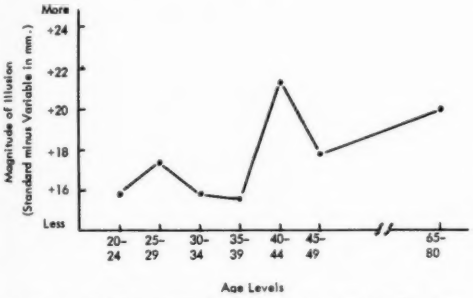

Fig. 2. Developmental changes in the Müller-Lyer illusion from ages 20 to 80.

significant differences among age groups from 20 through 39. The mean potency of the illusion for the 40-44 year group was significantly greater than for all other age groups with the exception of the 65-80 year group. The 45-49 year group differed only from the 40-44 year group; the 65-80 year group was significantly more susceptible to the illusion than age groups 20-24, 30-34 and 35-39.

These statistical findings confirm the generalization that susceptibility to the illusion is fairly constant between ages 20 and 39 and there is an increase of susceptibility between the ages of 40 and 80.

TITCHENER CIRCLES ILLUSION

Procedure. The Titchener Circles illusion, shown in Figure 3, consists of an inner circle surrounded by a concentric ring of circles. The

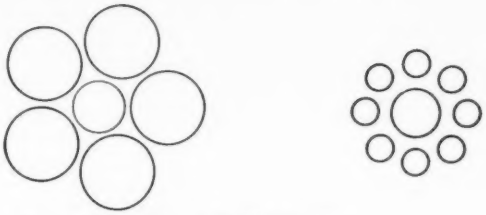

Fig. 3. The Titchener Circles pattern.

standard, always on the left, was composed of an inner circle, 16.5 mm. in diameter, and 5 surrounding circles each with a diameter of 25 mm. The inner circle of the variable varied from 9.00 to 21.00 mm. in steps of .75 mm. These variable circles were surrounded by 8 circles each, 9 mm. in diameter. *S* was presented with a chart on which were drawn 17 pairs containing the standard on the left and the variable on the right. At the top of the chart the inner circle of the variable configuration was smallest (9 mm. in diameter) and increased toward the bottom so that the variable of the pair lowest on the chart had the biggest inner circle, 21.00 mm. in diameter.

The task was to judge for each of the 17 pairs whether the center circle on the right (variable) was larger, equal, or smaller than the center circle on the left (standard). Two trials were given each *S*, i.e., in one trial *S* started from the top and moved down; in the other trial *S* started with the bottom pair and moved upward.

Utilizing the two series, the point of subjective equality (expressed in mm.) was calculated and served as the measure employed in the analysis. The results are presented in terms of difference between inner circles (standard

TABLE 1. AGE DIFFERENCES ON THE MÜLLER-LYER ILLUSION.

Age	Means (mm.)[a] (Standard minus Variable)	Differences between Means						
		20–24	25–29	30–34	35–39	40–44	45–49	65–80
20–24	+15.9	.....	1.4	0.0	0.3	5.6**	2.0	4.1*
25–29	+17.3	.....	.....	1.4	1.7	4.2*	0.6	2.7
30–34	+15.9	.....	.....	.....	0.3	5.6**	2.0	4.1*
35–39	+15.6	.....	.....	.....	.....	5.9**	2.3	4.4*
40–44	+21.5	.....	.....	.....	.....	.....	3.6*	1.5
45–49	+17.9	.....	.....	.....	.....	.....	.....	2.1
65–80	+20.0	.....	.....	.....	.....	.....	.....	.....

[a] A plus sign indicates that the variable was adjusted so that it was objectively shorter than the standard (illusion effective). The standard (angles inward) was 75 mm. long.

* $P < .05$.

** $P < .01$.

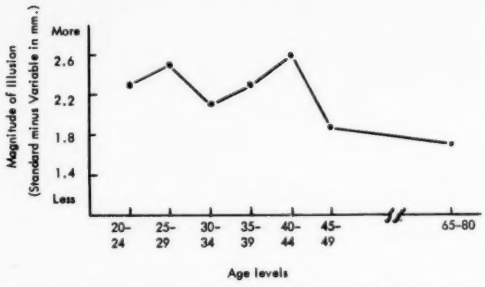

Fig. 4. Developmental changes in the Titchener Circles illusion from ages 20 to 80.

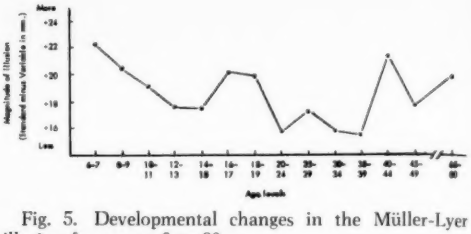

Fig. 5. Developmental changes in the Müller-Lyer illusion from ages 6 to 80.

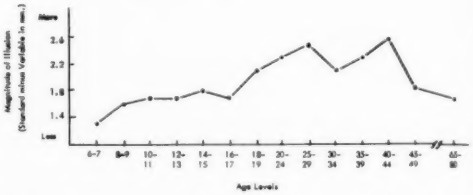

Fig. 6. Developmental changes in the Titchener Circles illusion from ages 6 to 80.

minus variable); a larger score represents greater susceptibility to the illusion.

Results. The results are represented in Figure 4, which shows the magnitude of the illusion (standard minus variable) for the various age levels. The graph shows that susceptibility to the illusion is fairly constant between ages 20 and 44 and decreases at the last two age levels, 45-49 and 65-80.

An analysis of variance performed on these data indicated that the source of variation between age groups (*MS* is 1.59 for 6 *df*), tested against the variation within age groups (*MS* is .60 for 93 *df*), was significant ($P < .05$). Table 2 shows the mean scores of the various age groups. There are no significant differences among the first five age levels (20-44). However, the difference is significant between age groups 45-49 and 40-44; and the oldest age group (65-80) is significantly different from age groups 20-24, 25-29, and 40-44.

Developmental changes, ages 6 to 80.

Müller-Lyer illusion. Figure 5 presents, in graphical form, the combined data on susceptibility to the Müller-Lyer illusion involving those data obtained in the present study for the 20-80-year-old groups and those data from the earlier study for 6-19-year-old groups. Aside from the increases in susceptibility at ages 16 through 19 and 40-44, the general picture from ages 6 through 80 is as follows: susceptibility to the illusion is most marked at the earlier age levels; it decreases with age, then increases once again at the oldest age levels.

Titchener Circles illusion. The developmental results for susceptibility to Titchener Circles illusion from ages 6 through 80, again using data from the earlier study, are presented in Figure 6. The curve indicates a fairly steady increase in the illusion effect from 6 through 44 years of age, followed by a decrease at the

TABLE 2. AGE DIFFERENCES ON THE TITCHENER CIRCLES ILLUSION.

Age	Means (mm.)[a] (Standard minus Variable)	Differences between Means						
		20–24	25–29	30–34	35–39	40–44	45–49	65–80
20–24	+2.34	.....	.12	.22	.07	.21	.45	.62*
25–29	+2.46	.....	.....	.34	.19	.09	.57	.74*
30–34	+2.12	.....	.....	.....	.15	.43	.23	.40
35–39	+2.27	.....	.....	.....	.....	.28	.38	.55
40–44	+2.55	.....	.....	.....	.....	.....	.66**	.83**
45–49	+1.89	.....	.....	.....	.....	.....	.....	.17
65–80	+1.72	.....	.....	.....	.....	.....	.....	.....

[a] A plus sign indicates that the variable chosen as perceptually equal was objectively smaller than the standard (illusion effective). The diameter of the standard circle (surrounded by large circles) was 16.5 mm.

* $P < .05$.
** $P < .01$.

two oldest age groups, 45-49 and 65-80 to a magnitude close to that found at the earliest age levels.

DISCUSSION

The developmental changes in the two illusions during the age span 6-80 years are opposed to each other in one respect but similar in another. In general, the trends are opposite insofar as there is an increase in susceptibility to one illusion at those points in the age span where there is a decrease in susceptibility to the other. The trends are similar insofar as with both illusions the changes that occur from the early to the middle years show a reversal from the middle to the later years.

These findings are in keeping with the assumption that the two illusions are based on different processes underlying the perception of part-whole relations. As stated earlier, the investigators assume that the Müller-Lyer illusion is based on a relationship of assimilation of parts: that is, there is assimilation of the horizontal lines to the total configuration. The decrease in susceptibility to the Müller-Lyer illusion from early to middle age is conceived to be a manifestation of decrease in global perception. This increases again at older ages. The Titchener Circles illusion, on the other hand, is assumed to be based on contrast between inner circle and surrounding set of circles. The increase in susceptibility to the Titchener Circles illusion between early and middle age is conceived to be a manifestation of increase of articulation of parts. This decreases again at older ages.

If one attempts to account for the developmental changes in the illusory effects in terms of increase in accuracy during the period of mental growth, and decrease in accuracy in old age, such an interpretation would be at variance with the obtained findings. The developmental change in one type of illusion is consonant with the notion of increasing accuracy: the other is in opposition to it. Both patterns may be accounted for, however, as noted above in terms of a "process" analysis, an analysis conceptualized in terms of the developmental law of increasing differentiation and hierarchic integration.[1]

In sum, then, the results indicate that perception of part-whole relationships in old age is formally similar to that which occurs at younger ages: i.e., these findings indicate greater globality and less articulation of parts at both old and young ages as compared with middle age. This formal similarity of perceptual behavior in young and old individuals is not restricted to perception of part-whole relations. In another study (Comalli, Wapner, & Werner, 1959) it has been demonstrated that there is also such regression in old age with respect to spatial organization. There it was shown that the effect of body tilt on perception of verticality is similar in old age to that which occurs in the young child; namely, a rod is seen as vertical when it is more closely aligned with the body. This is interpreted as greater egocentricity or the greater determination of the object world with the self as referent. Thus, in old age, there is decreased differentiation of self and world as manifested by greater egocentricity.

The present study, together with the earlier study of spatial organization just cited, demonstrates the fertility of developmental concepts for the analysis of behavioral changes occurring during the entire life span. The findings support the interpretation that through the entire life span there is progression which is followed by regression.[2] Both of these changes can be interpreted in terms of the following developmental law: Where there is progression it proceeds in terms of differentiation and hierarchic integration; in the obverse, regression, the shift is reverse, i.e., from more to less differentiation and hierarchic integration. These developmental concepts are applicable whether one deals with regression as a function of changes in chronological age (Comalli *et al.*, 1959), as a function of psychopathology (Carini, 1953; Wapner & Werner, 1957), or as due to more transient conditions such as drugs (Krus & Wapner, 1959) or conditions of stress (Lofchie, 1953). The fundamental problem still remains of identifying possible differences that may underlie the formally similar perceptual behavior occurring in early childhood, in old age, in psychopathological states, and under transient conditions such as drugs and stress.

[1] It may be noted that a number of other investigators such as Galli (1926), Piaget and his coworkers (1943, 1950), Rüssel (1934), and Walters (1942), have studied ontogenetic changes in one or the other two illusions used here, restricting themselves, however, to younger age levels. On the whole, their results are concordant with those of the present study with respect to these two illusions.

[2] It should be emphasized that, for us, "developmental regression" is not an evaluative concept which refers to a decrement or loss in performance. Such an evaluation in terms of loss is irrelevant from the viewpoint of the present analysis (cf. Birren, 1959).

SUMMARY

The present investigation deals with changes that occur in the perception of part-whole relationships from 6 through 80 years of age. The following age trends were found: (1) The Müller-Lyer illusion effect (based on assimilation of part to whole) is greatest for the youngest age group, declines to a minimum between 20 and 39 years of age, and increases again at older age levels. (2) The Titchener Circles illusion effect (based on contrast of parts to parts) increases from 6 through 44 years of age, and decreases at older age levels.

These results are interpreted in terms of developmental concepts of regression.

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A SUPPLEMENTARY REPORT ON AGE DIFFERENCES IN RETENTION OVER A TWENTY-FOUR HOUR PERIOD*

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A study reported by Wimer and Wigdor (1958) indicated that there may be no age loss in retention, as distinct from acquisition, when degree of original learning is controlled. In that experiment, the learning material consisted of four paired associates, and the retention interval was 15 minutes. The present study, using a longer learning task (seven paired associates) and a longer retention interval (24 hours), is an extension of the previous one.

METHOD

The subjects were 17 males over 65 (mean age, 71.9 years) and 20 males aged 18 to 29 (mean age, 20.3 years). The young subjects were college sophomores. The old subjects were college professors, prominent ministers, or carefully selected patients at a veterans' hospital or residents in a veterans' custodial home. For a more complete description of the subjects see Wimer (1960).

The learning task consisted of seven paired associates taken from a longer list of nonsense materials originally devised by Ruch (1934). The pairs consisted of the following nonsense products:

E x Z = G
H x Y = J
B x D = M
R x S = Q
W x L = S
K x U = T
F x P = V

The material was printed in letters one inch high and one-half inch wide in black ink on three-inch by five-inch white index cards and mounted in a Kardex book unit. The left side of the equation, the stimulus, was first presented with a "?" on the right side of the equal sign. The following card contained the complete equation. The stimulus and response cards were each presented for approximately three seconds, and the same interval was used between trials. The list was presented in three different orders to prevent serial learning of the response members. Learning was to the criterion of one perfect repetition. Retention was measured between 23 and 26 hours after original learning was completed.

RESULTS

The results of the experiment indicate that there are age losses in both (intentional) learning and recall. The average original learning scores and recall scores are presented in Table 1. The Mann-Whitney test was used to test the significance of the differences between the scores of the young and old groups for original learning and recall. As may be seen from the table, both differences are significant beyond the .01 level.

DISCUSSION

The results of the present experiment indicate that there is a significant age loss in retention over a 24-hour interval. The present results are not necessarily inconsistent with those obtained in the previous study. The difference between the two studies may be attributed to the longer retention interval used and the presumably more reliable scores on the longer learning task.

Since the results of the previous study and the findings of Gladis and Braun (1958) both indicate that advancing age does not increase susceptibility to the effects of retroactive inhibition, it is assumed that the obtained age loss in retention is due to factors other than retroaction. There are at least two other possible explanations: (a) proactive inhibition, and (b) failure in the consolidation process.

If it is assumed that the difference between these results and the results obtained in the previous experiment is due to increased precision of measurement in the present experiment, it would follow that an age loss in retention should be obtainable for the 15-minute interval as well as for the 24-hour interval. That is, there may be a uniform age loss for all reten-

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tion intervals. In this case, it is possible that the loss may be due to the effects of previous learning. It has been demonstrated by Underwood (1957) that proaction may be a more important factor in producing forgetting than has been realized. A greater amount of previous learning for the older group should increase the probability that retention of any given material will be subject to the effects of proactive inhibition. This hypothesis should be directly testable, for it predicts that, although the acquisition loss for the aged may be less for more familiar materials than for those which are ordinarily encountered less frequently (Ruch, 1934), the retention loss should be greater.

It is also possible that age losses in retention can be shown only for intervals of time greater than the 15-minute interval used in the previous experiment. The age loss in retention may be due to some defect in the consolidation process. It has been suggested (Hebb, 1949) that there are two kinds of memory traces. A reverberatory activity in the brain is proposed to maintain associations for a sufficient period of time for structural changes (*i.e.*, consolidation of the memory trace) to occur. Stellar (1957) reviewed evidence which might be taken to indicate that periods up to an hour may be required. If the age defect in retention is due to differences of the consolidative processes, a time interval greater than the 15-minute interval used in the previous experiment may be required before an age loss appears.

TABLE 1. AVERAGE SCORES FOR YOUNG AND OLD SUBJECTS.

	No. of Trials to Learn	No. of Items Recalled
Young	11.25	6.10
Old	25.29	4.76
Mann-Whitney test (z)	3.58*	2.71*

* Significant at or beyond the .01 level.

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A RESEARCH NOTE: EFFECTS OF DEXTRO-AMPHETAMINE AND MEPROBAMATE ON PROBLM-SOLVING AND MOOD OF AGED SUBJECTS*

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The purpose of this study was to explore the effects of meprobamate, dextro-amphetamine, and a placebo on the problem-solving performance and mood of aged subjects. It has been reported that, at dose levels from 400-800 mg., meprobamate does not affect psychomotor efficiency, visual acuity, depth perception, visual balance, motor steadiness, ability to make rapid judgments in simulated stress situations, or complex problem-solving ability (Marquis, Kelly, Miller, Gerard, & Rapaport, 1957; Reitan, 1957). Reitan found only a slight impairment of problem-solving ability and visual accuracy at four times the normal dosage. Kornetsky (1958) noted impairment in motor coordination, reaction time, and learning of adults at higher doses (1600 mg.) of meprobamate. At half this dosage only the rate of learning of his *Ss* was affected adversely. In the same study, 5 and 15 mg. of d-amphetamine did not affect performance significantly in any of the measured areas.

In contrast to the depressant action of meprobamate, d-amphetamine has been described as a "stimulant" drug which tends to elevate ego-strength and feelings of self-esteem (Straker, 1953). Small doses of the drug (5-10 mg.) administered to a group of elderly females (average age 78) were found to increase slightly feelings of well-being and energy level without causing untoward physical or physiological effects (Arnett & Harris, 1948). Bradley and Bowen (1940) found that d-amphetamine altered positively the emotional attitude of children toward unpleasant tasks resulting in increased intellectual performances.

METHOD

The 31 *Ss* were male veterans residing in the Domiciliary at the VA Center, Martinsburg, West Virginia. They were ambulatory, capable of self-care, and had been screened for psychiatric and organic brain disability. The age range was 59 to 83, with a mean of 65.5. Educational level ranged from no formal schooling to medical school graduation. Most of the men had been semi-skilled workers, although the group included two retired physicians, one lawyer, and a chemist.

Subjects were randomly assigned to one of three drug groups: 12 *Ss* received 400 mg. of meprobamate, 10 *Ss* received 5 mg. of d-amphetamine, and 9 *Ss* received a placebo (sodium bicarbonate, 5 mg.). Aside from the drugs, the experimental procedure was the same for each *S*.

On the first day the vocabulary section of the Shipley-Institute of Living Scale was administered, to provide a gross measure of intellectual level (Buros, 1949). This was followed by the problem-solving task, and finally by the Clyde Mood Scale (Clyde, 1960). On the second day each *S* received a drug; then, one hour later, repeated the problem-solving task and the Mood Scale.

The problem-solving task, described in earlier studies by Kay (1954) and Ross, Vicino, and Krugman (1960), is one of translating spatial perception into motor performance. The task is one in which the *S* finds the correct button to push each time that a different signal light is flashed on a board. The task is made progressively more difficult after each series of 10 trials. The number of errors for each trial provided the measure of problem-solving ability.

The Clyde Mood Scale consists of 133 items designed to measure six factors of mood: Friendly, Energetic, Clear-thinking, Aggressive, Jittery, and Depressed. The *S* is asked to sort the items (such as "Agreeable," "Lively," "Troubled") according to "how you feel today."

FINDINGS

Means and range of vocabulary scores for the three groups did not differ appreciably. The vocabulary age for the d-amphetamine

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group was approximately 15.7 years, 14.5 years for the placebo group, and 14.3 years for the meprobamate group.

An analysis of covariance, relating vocabulary scores and post-drug problem-solving error scores did not reveal significant differences between the groups. An analysis of covariance controlling for differences in pre-drug error scores did not yield significant differences between the groups in their post-drug problem-solving performances. A one-way analysis of variance by ranks for the three groups (post-drug error scores), and a median test for the placebo versus combined drug groups supported the conclusion that there were no significant differences between the groups in problem-solving performance. (Because of the limited range of problem-solving scores and the skewness of the data, the possibility of unreliability of scores was checked. The test-retest coefficients for the three groups ranged from .75 to .83. We concluded that the scores were adequately reliable for the purposes of this experiment.)

An analysis of covariance indicated that one possibly significant effect of the drugs and placebo preparations occurred on the "clear-thinking" score of the Clyde Mood Scale. (There were no before-after differences for the other five factors of mood.) The *Ss* felt somewhat less clear-thinking (less able to concentrate, less efficient, less alert) after meprobamate, and much less so after d-amphetamine, than after the pacebo.

Because these differences in feeling between the groups were not consistent with their actual problem-solving performance, it is conceivable that those *Ss* who received placebo improved in clear-thinking as a result of "placebo effect"; and that the somatic sensations produced by the drugs may have counteracted the "placebo effect" in the two drug groups. Future investigation is suggested, designed to answer the question of the uniqueness and addivity of pharmacologic and placebo effects.

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BOOK REVIEWS

Old Age and Political Behavior: A Case Study. By Frank A. Pinner, Paul Jacobs, and Philip Selznick. Berkeley: University of California Press, 1959. Pp. xi + 352. $6.00.

Pension movements as an expression of old age political behavior have never been comprehensively studied although they are indigenous to our culture alone. Most publications in the past have suffered from shallow conceptualizations or serious empirical weaknesses; too many have verged upon the sensational. Pinner and associates, however, have combined the disciplines of sociology, political science, and journalism in an empirical analysis of the McLain movement, officially called the California Institute for Social Welfare. This volume is one of a series produced under the aegis of the University of California's Bureau of Industrial Relations as part of a five-year interdisciplinary study of the problems of aging in an industrial society.

The authors employed a questionnaire to test differences and similarities in attitudes, beliefs, and behavior between two groups of old age assistance recipients, those who belonged to the Institute and those who did not. A very useful appendix contains the questions, an explanation of the sampling procedures and problems, and a quantitative statement of the responses. One of the authors maintained close personal contact with the Institute for approximately two years, conducting interviews with George W. McLain, its founder and leader, and with members of his staff.

Conceptually, the pension movement is viewed in this study as a phenomenon of emerging and dependent social groups. Isolation is the key concept employed in understanding the aged, their interrelationship with the pension promoter, and the degree of effectiveness with which the group presses its demands upon society. Isolated constituencies, low in status, are likely to be organized by marginal leaders. However, the marginal type of leader and the isolation of the group within the community inhibit the effectiveness of the pension movement and make it politically vulnerable.

Participation in the McLain movement by the aged is seen to lead to their increased estrangement from the social world. Upon the existing fact of social isolation is imposed a greater psychological isolation. One of the surprising findings of the study is that membership does not offer new and satisfying personal ties for the aged. This is explained in part by the reluctance of the pension leader to permit the development of clubs and to his conception of the organization as primarily a fund-raising device. The McLain pension movement is viewed as being composed of aged customers on the one hand, with no independent role, and "Uncle George," in whom complete ownership and control inhere.

Status-anxiety was revealed by the questionnaire to constitute the most significant attitude among old-age assistance recipients. The differences between the two groups of aged tested were found to be one of degree, not of kind. Institute members exhibited a higher degree of status-anxiety and were much more negativistic toward social workers and the old age assistance law.

The style and social attitude of the Institute is attributed to a high degree of participation therein by the "slightly-privileged" among the aged. It is the conclusion of the authors that the old age assistance law helps create a privileged group within the pension population —home owners, married couples with combined grants, individuals with additional income. They are the ones particularly sensitive to the appeal of the pension promoter.

The authors conclude that while separate organizations for the aged may be undesirable since they sharpen isolation, political pressure on behalf of the aged should be expected and accepted "as long as poverty and dependency are corollaries of retirement." No evidence is found that McLain has been able to weld his followers into a solid phalanx responding to his commands. It is clear that he cannot count upon their engaging in precinct organization or campaigning which are so necessary for the success of mass movements at the polls. In view of the crippling effect of isolation upon the pension movement, the authors recommend that "political activity on behalf of aged ought to become part of broader social welfare programs sponsored by groups that have a secure base in the organized community."

In this reviewer's opinion some of the recommendations are rather simple in nature, and not all of the conclusions based upon the questionnaire are confirmed by the data. At times contradictory conclusions are drawn from identical data. While no study should be expected to answer all the questions it proposes to examine, a number of the central ones are not touched upon. The introductory chapter poses the question of whether the aged are becoming segregated in our society and asks how far the process has gone. Nowhere do the authors offer a base point from which to measure increasing segregation, nor are these questions in any way resolved. Such problems, as well as the query of whether the aged develop values which are dominated by the life experience of old age, are perhaps more readily ascertainable by longitudinal approaches.

This study concerns itself with one pension movement, in one period of time, in one state, and with one stratum of aged. In all fairness to the authors, these points are made clear in the introductory chapters, and yet they become increasingly blurred in the study and are not adequately stressed in the summary and conclusion.

California is an atypical state and the behavior of its aged in a number of pension movements is atypical also. Is one to conclude from the absence of pension movements elsewhere that "status anxiety" is not the predominant psychological characteristic of the "aged poor" outside of California? Do the laws of other states inhibit or fail to create a highly sensitive discontented group of "slightly-privileged" among the recipients of old age assistance? Yet many of the characteristics of the California law are found elsewhere. How useful, then, are these conceptual tools in studying the aged in the rest of the country? Is it possible that political climate and style are the significant factors in determining whether pension promoters will emerge and pension movements materialize?

In effect, these questions constitute a plea for the further study of old age and political behavior. In their study of the California Institute of Social Welfare, Pinner and associates have made a worthwhile beginning in a long neglected field.

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Ensuring Medical Care for the Aged. By Mortimer Spiegelman. Homewood, Ill.: Richard D. Irwin, 1960. Pp. xiii + 280. $5.75.

Ensuring Medical Care for the Aged is a careful and thorough compilation of available data bearing on the problem of the financing of medical care for older persons in the United States. The book reviews the social and economic status of the aging, their attitudes toward health care, existing material on the utilization of medical care, and existing and proposed mechanisms for the financing of such care. In addition to making a full presentation of numerical data pertinent to the medical care problem, Mr. Spiegelman performs the useful service of evaluating these varied statistical materials. He clearly indicates the limitations and strengths of survey data, as well as the limitations of estimates based on population samples. He also points out some of the dangers inherent in estimating the utilization and costs of medical care plans when no actuarial experience is available as a basis for such estimates.

Within the last few years, medical care for the aged has become a topic of public interest. Protagonists of various points of view have published a number of statements about the aged and their medical care needs. Students of the social and economic status of older people in the United States have been hard put to reconcile the data presented in these often conflicting statements. For all those seriously interested in the health problems of older people, *Ensuring Medical Care for the Aged* should be required reading. It is a learned statement of the available facts in this controversial area by an internationally-known actuary and statistician.

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INDEX TO CURRENT PERIODICAL LITERATURE

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THE subject categories are those in *A Classified Bibliography of Gerontology and Geriatrics* by Nathan W. Shock published by Stanford University Press, Stanford, California (1951). Only major headings are used and the Roman numerals correspond to those given in the bibliography. In so far as possible, references are classified according to organ systems. Thus, most of the material on Geriatrics will be found under the organ system involved in the disease. Cross references are indicated by number at the end of each section. When available, abstract references are given (*B. A.—Biological Abstracts, P. A.—Psychological Abstracts,* and *P. I.—Population Index*). Abbreviations for journals are those used in *A World List of Scientific Periodicals Published in the years 1900-1933, 2nd Edition.* For journals not listed, abbreviations were devised according to the general rules used in the above source. It is impossible to cover all journals and list all papers concerned with aging and the aged. Authors and publishers are requested to call attention to publications or to send reprints to the Gerontology Branch, Baltimore City Hospitals, Baltimore 24, Maryland. The assistance of the Forest Park Foundation, Peoria, Illinois, in the preparation of these materials is gratefully acknowledged.

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